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## T cell-dependent antibody response to staphylococcal enterotoxin B.

Williams O, Aroeira LS, Mengel J.

Department of Immunology, Faculty of Medicine of Ribeirao Preto, University of Sao Paulo, Brazil.

Treatment of mice with staphylococcal enterotoxin B (SEB) induces specific T-cell tolerance to this superantigen, characterized by partial deletion of V beta 8+ T cells in vivo and T cell anergy in vitro. In this study we examined the humoral response to SEB in BALB/c mice. Immunization of mice with SEB results in a detectable anti-SEB antibody response. Upon further treatment of mice with SEB, specific antibody levels increase significantly and the response is accelerated--characteristics of a secondary humoral response. The secondary antibody response is T cell dependent, can be transferred to T cell deficient mice with splenocytes and is composed mainly of IgM, IgG1 and IgG2b isotypes, suggesting that Th2 cells provide B cell help in this response. These data demonstrate that at the same time as inducing in vitro unresponsiveness, SEB primes SEB-specific T helper cells to provide help for B cells in a secondary antibody response.

PMID: 7660063 [PubMed - indexed for MEDLINE]

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=> s conjugate  
L1 230847 CONJUGATE

=> s l1 and branching groups  
L2 1 L1 AND BRANCHING GROUPS

=> d l2 cbib abs

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN  
1994:264827 Document No. 120:264827 Metal chelating peptide. Gariepy, Jean  
(Ontario Cancer Institute, Can.). PCT Int. Appl. WO 9323425 A1 19931125,  
25 pp. DESIGNATED STATES: W: JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR,  
IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO  
1993-CA207 19930507. PRIORITY: US 1992-880691 19920508.  
AB A branched peptide carrying a number of chelating groups (metal chelating  
peptide (MCP)) has a C-terminus that may be structured to provide a  
variety of means for unidirectional coupling to a targeting agent such as  
an antibody. The number of metal chelating sites may be quite large (in  
excess of 16). The MCP can be used to deliver a concentrated radionuclide mass  
to a target cell by coupling the MCP to a targeting agent. A branched  
peptide with a C-terminal  $\beta$ -alanine was synthesized by t-Boc chemical  
with branches introduced by coupling to  $\epsilon$ -amino groups of lysine  
and EDTA moieties added as the t-Bu protected derivative Methods for coupling  
the protein to antibodies via the carbohydrate moiety using a maleimide  
are discussed.

=> s l1 and polymer  
L3 11373 L1 AND POLYMER

=> s l3 and branch  
L4 60 L3 AND BRANCH

=> dup remove l4  
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L5 40 DUP REMOVE L4 (20 DUPLICATES REMOVED)

=> d l5 1-40 cbib abs

L5 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

2004:182901 Document No. 140:241090 Synthetic heparin-binding growth factor analogs. Pena, Louis A.; Zamora, Paul O.; Lin, Xinhua; Glass, John D. (Biosurface Engineering Technologies, Inc., USA; Brookhaven Science Associates, LLC). PCT Int. Appl. WO 2004018499 A2 20040304, 74 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US26189 20030820. PRIORITY: US 2002-224268 20020820; US 2003-644703 20030819.

AB The invention provides synthetic heparin-binding growth factor analogs having at least one peptide chain, and preferably two peptide chains branched from a dipeptide **branch** moiety composed of two trifunctional amino acid residues, which peptide chain or chains bind a heparin-binding growth factor receptor and are covalently bound to a non-signaling peptide that includes a heparin-binding domain, preferably by a linker, which may be a hydrophobic linker. The synthetic heparin-binding growth factor analogs are useful as pharmaceutical agents, soluble biologics or as surface coatings for medical devices.

L5 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

2004:372847 Document No. 140:363102 Synthetic heparin-binding growth factor analogs. Pena, Louis A.; Zamora, Paul O.; Lin, Xinhua; Glass, John D. (USA). U.S. Pat. Appl. Publ. US 2004087505 A1 20040506, 36 pp., Cont.-in-part of U.S. Ser. No. 224,268. (English). CODEN: USXXCO. APPLICATION: US 2003-644703 20030819. PRIORITY: US 2002-224268 20020820.

AB The invention provides synthetic heparin-binding growth factor analogs having at least one peptide chain, and preferably two peptide chains branched from a dipeptide **branch** moiety composed of two trifunctional amino acid residues, which peptide chain or chains bind a heparin-binding growth factor receptor and are covalently bound to a non-signaling peptide that includes a heparin-binding domain, preferably by a linker, which may be a hydrophobic linker. The synthetic heparin-binding growth factor analogs are useful as pharmaceutical agents, soluble biologics or as surface coatings for medical devices.

L5 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

2004:301272 Mechanical spectroscopy of thin layers of PPV **polymer** on Si substrates. Nagy, A.; Strahl, A.; Neuhauser, H.; Schrader, S.; Behrens, I.; Peiner, E.; Schlachetzki, A. (Institute for Metal Physics and Nuclear Solid State Physics, Technical University of Braunschweig, Braunschweig, Germany). Materials Science & Engineering, A: Structural Materials: Properties, Microstructure and Processing, A370(1-2), 311-315 (English) 2004. CODEN: MSAPE3. ISSN: 0921-5093. Publisher: Elsevier Science B.V..

AB The vibrating reed technique with electro"static" excitation and optical detection has been applied to investigate thin layers of poly-phenylene-vinylene, deposited by spin coating onto microfabricated Si cantilevers, during temperature cycling programs between 90 and 540 K at a rate of 1 K/min. From the vibration frequencies the Young's modulus of the film can be estimated to be about 10 MPa at room temperature in the precursor phase

(if prepared from a solution in toluene), which increases by conversion to the **conjugate** bonded **polymer** to about 50 MPa. The temperature dependence of internal friction reveals the processes of  $\gamma$  relaxations (crankshaft motion of side **branches** in the precursor) and  $\beta$ -relaxation (movements of a few monomer blocks in the **polymer** chain), as well as peaks indicating the structural transformations during conversion, and possibly a glass transition in the amorphous precursor phase. After conversion only the  $\beta$ -relaxation

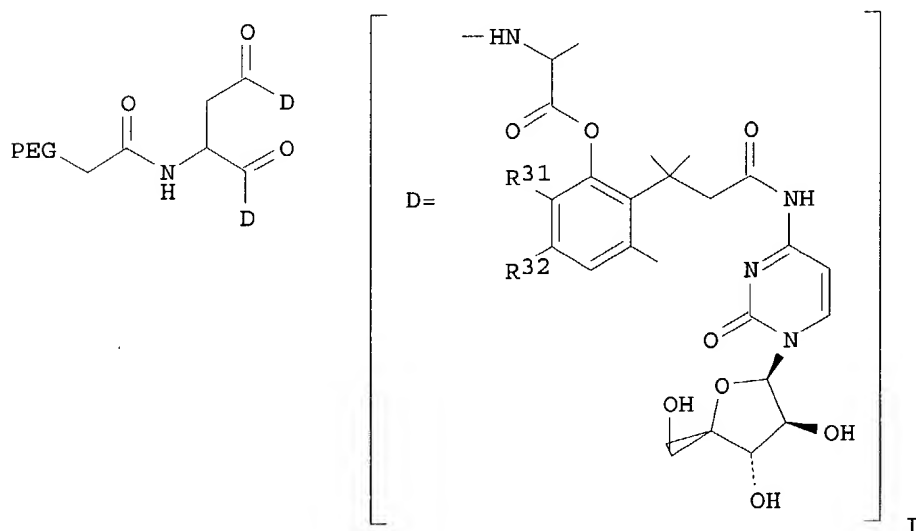


persists.

- L5 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN  
2003:675923 Document No. 139:222511 Organic field-effect transistors. Okamura, Hisashi (Fuji Photo Film Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 2003243660 A2 20030829, 14 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 2002-35383 20020213.
- AB The title transistors contain gate insulator films and semiconductor active layers which are made of super-branched **polymers** that have the structures in which plural number of organic groups are **branch**-like bonded. The branching parts or the outermost shells of **branch** ends contain condensation-ring-type aromatic residual groups, complex ring aromatic residual groups or aromatic amine residual groups.
- L5 ANSWER 5 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN  
2003387671 EMBASE Controlled Release Society - 30th Annual Meeting and Exposition: 19-23 July 2003, Glasgow, Scotland, UK. Furness G.. G. Furness, Brackens, Dodds Bottom, Nutley, East Sussex TN22 3LX, United Kingdom. guy.furness@btopenworld.com. IDrugs 6/9 (862-864) 1 Sep 2003. ISSN: 1369-7056. CODEN: IDRUFN. Pub. Country: United Kingdom. Language: English. Summary Language: English.
- AB The few technologies described here give a sense of the CRS Meeting as a showcase of cutting-edge research. It is clear that drug-delivery scientists are taking a step further than, for example, simply wrapping formulations in standard gelatin capsules, or delivering standard dry powders to the lung through standard inhalers. Strands of knowledge and experience from other **branches** of science, such as molecular biology, biotechnology, nanotechnology, advanced **polymer** chemistry and electronic engineering, are being brought together in novel applications. Also of note is that much of the research presented at the meeting was carried out in collaborations between industry and academia.
- L5 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN  
2003:127188 Document No. 138:316855 Macromolecular MRI Contrast Agents with Small Dendrimers: Pharmacokinetic Differences between Sizes and Cores. Kobayashi, Hisataka; Kawamoto, Satomi; Jo, Sang-Kyung; Bryant, Henry L., Jr.; Brechbiel, Martin W.; Star, Robert A. (Metabolism Branch, National Institutes of Health, National Cancer Institute, Center for Cancer Research, Bethesda, MD, USA). Bioconjugate Chemistry, 14(2), 388-394 (English) 2003. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.
- AB Large macromol. MRI contrast agents with albumin or dendrimer cores are useful for imaging blood vessels. However, their prolonged retention is a major limitation for clin. use. Although smaller dendrimer-based MRI contrast agents are more quickly excreted by the kidneys, they are also able to visualize vascular structures better than Gd-DTPA due to less extravasation. Addnl., unlike Gd-DTPA, they transiently accumulate in renal tubules and thus also can be used to visualize renal structural and functional damage. However, these dendrimer agents are retained in the body for a prolonged time. The purpose of this study was to obtain information from which a macromol. dendrimer-based MRI contrast agents feasible for use in further clin. studies could be chosen. Six small dendrimer-based MRI contrast agents were synthesized, and their pharmacokinetics, whole-body retention, and dynamic MRI were evaluated in mice to determine an optimal agent in comparison to Gd-[DTPA]-dimeglumine. Diaminobutane (DAB) dendrimer-based agents cleared more rapidly from the body than polyamidoamine (PAMAM) dendrimer-based agents with the same nos. of **branches**. Smaller dendrimer **conjugates** were more rapidly excreted from the body than the larger dendrimer **conjugates**. Since PAMAM-G2, DAB-G3, and DAB-G2 dendrimer-based contrast agents showed relatively rapid excretion, these three **conjugates** might be acceptable for use in further clin. applications.

L5 ANSWER 7 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN  
 2002:657977 Document No. 137:206540 Terminally-branched polymeric linkers  
 and polymeric **conjugates** as prodrugs. Choe, Yun Hwang;  
 Greenwald, Richard B. (Enzon, Inc., USA). PCT Int. Appl. WO 2002066066 A1  
 20020829, 57 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA,  
 BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,  
 ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,  
 KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,  
 OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW:  
 AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR,  
 IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English).  
 CODEN: PIXXD2. APPLICATION: WO 2002-US4780 20020219. PRIORITY: US  
 2001-PV272511 20010220.

GI



AB Terminally-branched polymeric prodrug platforms capable of high degrees of loading are disclosed. In preferred aspects of the invention, the prodrug platform releases multiple parent compds. after each **branch** holding the active agent undergoes a benzyl elimination reaction. E.g., I was prepared and antitumor activity was tested in mice.

L5 ANSWER 8 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN  
 2002:657915 Document No. 137:206534 Terminally-branched polymeric linkers  
 and polymeric **conjugates** as prodrugs. Choe, Yun Hwang;  
 Greenwald, Richard B. (Enzon, Inc., USA). PCT Int. Appl. WO 2002065988 A2  
 20020829, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA,  
 BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,  
 ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,  
 KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ,  
 OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW:  
 AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR,  
 IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English).  
 CODEN: PIXXD2. APPLICATION: WO 2002-US4781 20020219. PRIORITY: US  
 2001-PV270009 20010220.

AB Terminally-branched polymeric prodrug platforms capable of high degrees of loading are disclosed. In preferred aspects of the invention, the prodrug platform releases multiple parent compds. after each **branch** holding the active agent undergoes a benzyl elimination reaction. Methods

of preparing the prodrugs and using the same in the treatment of mammals are also disclosed. For example, a polyethylene glycol-cytosine arabinoside (PEG-Ara-C) **conjugate** was prepared. The PEG-Ara-C **conjugate** demonstrated in tumor-bearing mice about equivalent antitumor activity with native Ara-C at only 20% of the active parent compound's dose. The IC50 for the PEG-Ara-C **conjugate** and the native Ara-C was 448 and 10 nM, resp., as determined in vitro using the P388/0 (murine lymphoid neoplasm) cell line.

L5 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

2002:539578 Document No. 137:106078 Surface modified semiconductive and metallic nanoparticles having enhanced dispersibility in aqueous media. Adams, Edward William; Bruchez, Marcel Pierre, Jr. (Quantum Dot Corporation, USA). PCT Int. Appl. WO 2002055186 A2 20020718, 46 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US42699 20011012. PRIORITY: US 2000-PV240216 20001013; US 2001-841237 20010423.

AB Water-dispersible nanoparticles are prepared by applying a coating of a multiply amphipathic dispersant to the surface of a hydrophobic nanoparticle comprised of a semiconductive or metallic material. The multiply amphipathic dispersant has two or more hydrophobic regions and two or more hydrophilic regions, and is typically polymeric. Preferred polymeric dispersants are comprised of (1) a hydrophobic backbone with hydrophilic **branches**, (2) a hydrophilic backbone with hydrophobic **branches**, or (3) a backbone that may be either hydrophobic or hydrophilic, and substituted with both hydrophilic and hydrophobic **branches**. Monodisperse populations of water-dispersible nanoparticles are also provided, as are **conjugates** of the water-dispersible nanoparticles with affinity mols. such as peptides, oligonucleotides, and the like.

L5 ANSWER 10 OF 40 MEDLINE on STN

DUPLICATE 1

2002271013. PubMed ID: 12009948. Evaluation of different alpha-Galactosyl glycoconjugates for use in xenotransplantation. Byrne Guerard W; Schwarz Alexander; Fesi Joanna R; Birch Patrick; Nepomich Anna; Bakaj Ivona; Velardo Margaret A; Jiang Cong; Manzi Adriana; Dintzis Howard; Diamond Lisa E; Logan John S. (Nextran Inc., 303B College Road, Princeton, New Jersey, USA.. gbyrne@nextran.com). Bioconjugate chemistry, (2002 May-Jun) 13 (3) 571-81. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB Porcine organs are rapidly rejected after transplantation into primate recipients due to the presence of preexisting immunoglobulins that bind to terminal galactose alpha1,3 galactose residues (alpha-galactosyl) present on porcine glycoproteins and glycolipids. Currently available immunosuppressive reagents have been largely ineffective at controlling the synthesis of these anti-Gal antibodies. Nonantigenic hapten **polymers** have been shown to be effective materials for blocking humoral immune responses in various model systems. We have developed a series of alpha-galactosyl glycoconjugate **polymers** and tested their ability to block anti-Gal antibody binding in vitro and in vivo. A galactose alpha1,3 galactose beta 1,4 GlcNAc trisaccharide free acid (TRFA) with a hexanoic acid spacer, containing five methylene groups and a carboxylic acid, was produced and coupled to a variety of polymeric backbones including dextran, branched poly(ethylene glycol) (PEG), and poly-L-lysine. The ability of monomeric TRFA and the alpha-galactosyl **conjugates** to block anti-Gal IgG and IgM binding was determined using a competition ELISA assay on defined HSA-Gal glycoconjugates and porcine microvascular endothelial cell substrates. We show that branched

PEG carriers, with a TRFA sugar attached to each **branch**, exhibit enhanced antibody blocking ability compared to TRFA, but at higher target antigen densities these simple PEG **conjugates** are no more effective than an equivalent amount of TRFA in blocking anti-Gal IgM antibody interactions. In contrast, **polymers** of the branched PEG **conjugates** and linear **conjugates** made using dextran and poly-L-lysine were 2000 to 70000-fold more effective inhibitors of anti-Gal antibodies. In a study using nonhuman primates, a single dose infusion of polymeric PEG or dextran glycoconjugates dramatically reduced the level of circulating anti-Gal antibodies in cynomolgus monkeys for at least 72 h. Glycoconjugates similar to these might be useful both to block anti-Gal interactions in vivo and to specifically control the induced anti-Gal immune response.

L5 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

2001:78410 Document No. 134:147856 Preparation of polypeptide dendrimers as unimolecular carriers of diagnostic imaging contrast agents, bioactive substances and drugs. Verdini, Antonio (Italy). PCT Int. Appl. WO 2001007469 A2 20010201, 33 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, BG, BR, CA, CH, CN, CU, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP7022 20000721. PRIORITY: IT 1999-FO15 19990723.

AB The invention describes new polypeptide dendrimers and processes for their synthesis. The polypeptide dendrimers of the invention have a structure which consists of a multifunctional core moiety from which highly branched polypeptide chains, formed by short peptide branching units, extend radially outwards. The outermost **branches** surround a lower d. space with hollows and channels into which bioactive substances employed in diagnosis and therapy can be entrapped or covalently linked. The said polypeptide dendrimers are particularly useful in a number of areas in biol. and medicine as carriers for the delivery of bioactive substances, including drugs, or as carriers of bacterial, viral and parasite antigens, gene-therapy compds. and diagnostic imaging contrast agents. N[CH<sub>2</sub>CH<sub>2</sub>NHCOCH(CH<sub>2</sub>Ph)NH-Gly-Gly-Orn(Boc)-Gly-Boc]<sub>2</sub><sub>3</sub> (Boc = tert-butoxycarbonyl) is an example of a polypeptide dendrimer which was synthesized. Various properties of the polypeptide dendrimers were studied, including stability to enzymic hydrolysis in vitro and immunogenicity in mice and its adjuvanticity when some of the NH<sub>2</sub> groups are covalently linked to the octapeptide antigen Ala-Asn-Pro-Asn-Ala-Asn-Pro-Asn.

L5 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

2001:895576 Document No. 136:25110 Hyperbranched polymeric micelles for encapsulation and delivery of hydrophobic molecules. Uhrich, Kathryn E. (Rutgers University, USA). U.S. US 6328988 B1 20011211, 11 pp., Cont.-in-part of U.S. Ser. No. 298,729. (English). CODEN: USXXAM. APPLICATION: US 1999-422295 19991021. PRIORITY: US 1999-298729 19990423.

AB Polymeric micelles for encapsulation of hydrophobic mols. are provided. Methods and formulations for delivering hydrophobic mols. to a host via these micelles are also provided. Methods of stabilizing liposomes or lipid based formulations by addition of polymeric micelles are also provided. Mucic acid hexyl ester core **polymer** with PEG 5000 **branches** was prepared as a white solid having a T<sub>m</sub> of 61° and a Mw of 17,800 Daltons (yield = 17%). The amount of lidocaine mol that can be entrapped within the polymeric micelles (the encapsulation number) was 1.0. The in vitro degradation of polymeric mycells was studied.

L5 ANSWER 13 OF 40 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

2002:13910 The Genuine Article (R) Number: 503UW. Biomaterials for molecular electronics development of optical biosensor for retinol. Ramanathan K

(Reprint); Svitel J; Dzgoev A; Sundaram P V; Danielsson B. Lund Univ, Dept Pure & Appl Biochem, Ctr Chem & Chem Engr, Box 124, S-22100 Lund, Sweden (Reprint); Lund Univ, Dept Pure & Appl Biochem, Ctr Chem & Chem Engr, S-22100 Lund, Sweden; Voluntary Hlth Serv, Ctr Prot Engr & Biomed Res, Madras 600113, Tamil Nadu, India. APPLIED BIOCHEMISTRY AND BIOTECHNOLOGY (OCT-DEC 2001) Vol. 96, No. 1-3, pp. 277-291. Publisher: HUMANA PRESS INC. 999 RIVERVIEW DRIVE SUITE 208, TOTOWA, NJ 07512 USA. ISSN: 0273-2289. Pub. country: Sweden; India. Language: English.

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Molecular electronics involves expertise from several **branches** of science. Various biomaterials and electronics are involved in the fabrication of such devices. While passive biomaterials are involved in anchoring the active biomolecules, the latter are involved in switching and/or signal transduction. In the present investigation we have used a glass-capillary-based approach to design a biosensor for retinol. The sensing element is retinol-binding protein (RBP). The affinity of retinoic-acid-horseradish peroxidase (**conjugate**) to RBP is tested using a surface plasmon resonance technique. A simple photomultiplier-tube-based system is exploited to monitor the chemiluminescent signal generated upon reaction of hydrogen peroxide and luminol with the **conjugate** bound to RBP. The photomultiplier tube is directly coupled to a computer for data logging.

L5 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN  
2001:3825 Document No. 134:290612 Synthesis of human proinsulin C-peptide and preparation of specific antibody to it. Li, Mo-Yi; Liu, Zhi-Hui; Shao, Xiao-Xia; Xia, Qi-Chang; Zhou, Guo-Ming; Lin, Qi-Shui; Cui, Da-Fu (Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, the Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China). Shengwu Huaxue Yu Shengwu Wuli Xuebao, 32(6), 665-668 (Chinese) 2000. CODEN: SHWPAU. ISSN: 0582-9879. Publisher: Shanghai Kexue Jishu Chubanshe.

AB A HPLC and CE pure human proinsulin C-peptide was synthesized by solid-phase method and TSK column purification Its amino acid sequence and MS were consistent with theor. values. In comparison with the formly reported chemical synthesis of C-peptide, this method has the advantage of simplicity and higher overall yield (41% ). To improve the immunogenicity and specificity of oligopeptide antibody, the acryloyl-C-peptides were transformed into a **polymer**; the product had a poly-propionyl-core matrix with C-peptide **branches**. This treatment gave a macromol. with a M, about 25 kD. By using the **polymer** to immunize New Zealand rabbits for 30 days, specific antiserum was obtained with titer of  $2.5 \times 10^4$  (by ELISA) , which did not cross react with BSA. Thus, the poly-propionyl-peptide system provided a new approach for preparing synthetic peptide antibody and therefore is promising for the preparation of synthetic peptide-based vaccine.

L5 ANSWER 15 OF 40 MEDLINE on STN DUPLICATE 2  
2000469424. PubMed ID: 10898569. Conjugation of epitope peptides with SH group to branched chain polymeric polypeptides via Cys(Npys). Mezo G; Mihala N; Andreu D; Hudecz F. (Research Group of Peptide Chemistry, Hungarian Academy of Sciences, Eotvos L. University, H-1518, Budapest, Hungary. ) Bioconjugate chemistry, (2000 Jul-Aug) 11 (4) 484-91. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB Since bioconjugates may play an important role as therapeutics in the future, the development of new and effective conjugation strategies is necessary. For the attachment of peptide-like molecules to carriers, there are two main coupling methods involving amide or disulfide bonds. Conjugation through an amide bond can be achieved in several well-defined ways known from peptide chemistry. However, the formation of disulfide bridges between cysteine-containing peptides and carrier molecules still has some problems. In this paper, we describe a novel approach in which the carrier polypeptide is modified by 3-nitro-2-pyridinesulfonyl (Npys)-protected cysteine and this derivative has been applied for

conjugation of Cys-containing epitope peptides with poly(L-lysine)-based branched polypeptides. Considering the stability of Npys group in the presence of pentafluorophenol, Boc-Cys(Npys)-OPfp derivative was selected for introduction to the N-terminal of **branches** of polypeptides backbone. The **branches** of the **polymers** were built up from oligo(DL-alanine) (poly[Lys(DL-Ala(m))], AK) and elongated by an optically active amino acid [poly[Lys(X(i)-DL-Ala(m))], XAK]. We found that the nature of X (Glu, Ser, Thr) has great influence on the incorporation of the protected cysteine residue. Herpes simplex virus and adenovirus epitope peptides were conjugated to Boc-Cys(Npys)-modified polypeptides. Results indicate that the incorporation of epitope peptides depends on the number of Npys group on the **polymers** as well as on the presence/absence of Boc-protecting group on the Cys residue. This new class of Cys(Npys)-derivatized branched polypeptides is stable for a couple of months and suitable for effective preparation of epitope peptide **conjugates** possessing increased water solubility.

- L5 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN  
 2001:21215 Document No. 135:205942 Molecular recognition using bioconjugate **polymers**. Maeda, Mizuo (Dep. Applied Chem., Kyushu Univ., Fukuoka, 812-8581, Japan). Chromatography, 21(4), 292-293 (Japanese) 2000. CODEN: CHROFZ. ISSN: 1342-8284. Publisher: Society for Chromatographic Sciences.
- AB A review with 4 refs. Capillary electrophoresis is an ideal method for gene anal., because the method can be performed with trace amount of samples, high resolution and shorter running time. We describe here an effect of oligonucleotide, which was introduced in poly(acrylamide) as a **branch**, on the recognition of an overall sequence of sample DNA fragments: Anti-sense sequence of c-K-ras codon 11-12 (5'-ACCAGC-3') was immobilized on poly(acrylamide) chain. The detection peak for c-K-ras codon 10-13 (5'-GGAGCTGGC-3'), which is complementary partner of the affinity ligand, was found to be retarded so that one base mutant having the sequence of 5'-GGAGCTAGTGGC-3' was clearly separated from the wild type. This method would allow quant. determination of normal and mutant genes at the same time online.

- L5 ANSWER 17 OF 40 MEDLINE on STN DUPLICATE 3  
 2000475063. PubMed ID: 10925454. Hepatic chemoembolization: clinical and experimental correlation. Wallace S; Kan Z; Li C. (Department of Radiology, University of Texas M.D. Anderson Cancer Center, Houston 77030, USA. ) Acta gastro-enterologica Belgica, (2000 Apr-Jun) 63 (2) 169-73. Ref: 20. Journal code: 0414075. ISSN: 0001-5644. Pub. country: Belgium. Language: English.
- AB Chemoembolization has become the preferred treatment for patients with inoperable, hypervascular hepatic malignancies in the Far East, but controversial elsewhere. In vivo microscopy in addition to other experimental procedures are used in this presentation to better understand the mechanisms involved in chemoembolization. In chemoembolization Lipiodol acts as a contrast material, a vehicle for chemotherapy and an embolic agent. Although not optimal, Lipiodol injected into the hepatic artery, traverses the peribiliary plexus to the portal veins resulting in a dual embolization. Chemoembolization creates ischemia, slows arterial flow and increases the contact time between the infusate and the neoplasms, increasing the tumor cell kill. However, the vascular occlusion also produces infarction and fibrosis compounding the already existing cirrhosis frequently associated with hepatocellular carcinoma. Lipiodol/ethanol (3:1) injected into the segmental or lobar hepatic artery supplying the neoplasm also gains access to the associated portal venous **branches** causing focal ablation. This preoperative approach is easier to perform than direct portal vein occlusion, with less parenchymal damage and comparable hypertrophy of the remnant liver frequently necessary for adequate hepatic function following resection. **Polymer-drug conjugates**, e.g. PG-TXL, have considerable potential for intra-arterial delivery especially with the dramatic increase in concentration of the drug in the tumor and its efficacy.

Using in vivo microscopy especially with green fluorescent protein (GFP) gene as an efficient and non-toxic tumor cell marker, the events leading to hepatic metastases can be documented which will serve to better evaluate these varied techniques of chemoembolization.

L5 ANSWER 18 OF 40 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 4

2000136695 EMBASE Conjugation of HS-oligopeptides with polymeric branched chain polypeptides containing multiple amino groups. Nagy I.B.; Dancs A.; Koczán G.; Mezo G.; Hudecz F.. F. Hudecz, Research Group for Peptide Chemistry, Hungarian Academy of Science, Eötvös L. University, P.O. Box 32, Budapest 112, H-1518, Hungary. Journal of Bioactive and Compatible Polymers 15/2 (139-154) 2000.

Refs: 31.

ISSN: 0883-9115. CODEN: JBCPEV. Pub. Country: United States. Language: English. Summary Language: English.

AB For the preparation of bioconjugates containing polymeric polypeptides with well-defined structure and composition, we systematically studied 3-(2-pyridyldithio)propionic acid N-hydroxy-succinimide ester (SPDP). SPDP as amino- and thiol-reactive heterobifunctional coupling agent is mainly used for protein-based **conjugates**, and very little data are available on its application for the modification of **polymers**. In this communication, we describe the effect of **polymer**/oligopeptide structure and of the reaction condition on the incorporation of oligopeptides with free thiol group (CAVKDEL, CTGRGDSP) into polymeric polypeptides possessing multiple amino groups. For these studies, linear poly[L-lysine] with free  $\epsilon$ -amino groups and its XAK-type branched polypeptide derivatives {poly[Lys(X(i)-DL-Ala(m))] ( $i < 1$ ,  $m \approx 3$ , XAK)} either with polycationic character {X = .diameter. (AK), X = Ser (SAK)} or with amphoteric nature {X = Glu (EAK)} were utilized. First, the **polymers** were modified with SPDP under various conditions, and the degree of substitution was determined. We found that the efficacy of the nucleophilic substitution of NH<sub>2</sub> groups with SPDP depended not only on the pH and the concentration of the coupling reagent but also on the **polymer** composition, mainly on the pK<sub>a</sub> of the **branch**-terminal amino group of the **polymers**. SPDP-modified polymeric polypeptides were reacted with the HS- oligopeptides, and the effects of **polymer**/oligopeptide structure as well as the reaction conditions (pH, peptide/(SSP)**polymer** molar ratio) on the composition of the product were evaluated. The results suggest that acidic pH is more favorable for the thiol-disulphide exchange, and the side chain composition of the **polymers** had a pronounced effect while the chemical structure of oligopeptides had only moderate influence on the average degree of substitution.

L5 ANSWER 19 OF 40 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
2000:59435 The Genuine Article (R) Number: 274AB. Synthesis and conformational studies of poly(L-lysine) based branched polypeptides with Ser and Glu/Leu in the side chains. Mezo G (Reprint); Remenyi J; Kajtar J; Barna K; Gaal D; Hudecz F. HUNGARIAN ACAD SCI, RES GRP PEPTIDE CHEM, POB 32, H-1518 BUDAPEST 112, HUNGARY (Reprint); LORAND EÖTVÖS UNIV, DEPT ORGAN CHEM, BUDAPEST, HUNGARY; NATL INST ONCOL, BUDAPEST, HUNGARY. JOURNAL OF CONTROLLED RELEASE (3 JAN 2000) Vol. 63, No. 1-2, pp. 81-95. Publisher: ELSEVIER SCIENCE BV. PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. ISSN: 0168-3659. Pub. country: HUNGARY. Language: English.  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB In a new group of polypeptides, the **branches** were composed of DL-Ala oligopeptide, L-serine and L-leucine or L-glutamic acid residues. The synthesis of eight different side-chain combinations is described. In the first group, Ser was attached directly to the epsilon-amino groups of polylysine, and Leu or Glu was situated at the side chain end (poly[Lys(X-i-DL-Ala(m)-Ser(j))]). Alternatively, Leu or Glu was positioned next to the polylysine backbone (poly[Lys(Ser(j)-DL-Ala(m)-X-i)], where X=L-Leu or L-Glu and m similar to 3-6, i less than or equal to 1 and j less than or equal to 1). The second group of **polymers**

was synthesised by grafting oligo(DL-alanine) chains to the E-amino groups of polylysine, followed by coupling of Ser and Leu or Glu consecutively to the chain ends, however, in a different order, resulting in the **polymers** (poly[Lys(X-i-Ser(j)-DL-Ala(m))]) and poly[Lys(Ser(j)-X-i-DL-Ala(m))], where X=L-Leu or L-Glu and m similar to 3-6, i less than or equal to 1 and j less than or equal to 1). The effect of amino-acid composition and sequence of side chains in branched polypeptides on solution conformation was studied by CD spectroscopy. CD spectra recorded in aqueous solutions of various pH (2-11) and ionic strengths (0.02-2.0 M NaCl) suggest that leucine- and serine-containing polypeptides have more ordered (alpha-helical) structure than the **polymers** with glutamic acid and serine residues in the same position. The influence of serine residues on ordered structure (helical or beta-sheet) formation depends on its position in the side chain as well as on the nature of amino acid X (Leu or Glu). The incorporation of Ser into the **branches** resulted in polypeptides possessing prolonged shelf stability and high water-solubility. No toxic effect of this new class of **polymers** was observed on mouse spleen cells, even after 4 h of incubation. (C) 2000 Elsevier Science B.V. All rights reserved.

L5 ANSWER 20 OF 40 MEDLINE on STN DUPLICATE 5  
 1999433850. PubMed ID: 10502343. Carrier design: new generation of polycationic branched polypeptides containing OH groups with prolonged blood survival and diminished in vitro cytotoxicity. Hudecz F; Pimm M V; Rajnavolgyi E; Mezo G; Fabra A; Gaal D; Kovacs A L; Horvath A; Szekerke M. (Research Group of Peptide Chemistry, Hungarian Academy of Sciences, Budapest 112, POB 32, H-1518, Budapest, Hungary.. fhudecz@ludens.elte.hu) . Bioconjugate chemistry, (1999 Sep-Oct) 10 (5) 781-90. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB For the construction of macromolecule-drug **conjugates**, it is important to provide rational basis to the selection of proper carrier. With respect to the importance of the side-chain structure and charge of the branched polypeptides in biological properties, we have prepared a new class of branched polypeptides with single or multiple hydroxyl groups and studied their solution conformation, in vitro cytotoxicity, biodistribution, and immunoreactivity. For comparative studies, polypeptides were designed to contain serine at various positions of the side chains, varying also the number. Ser was attached to the end of oligo(DL-Ala) side chains grafted to polylysine resulting polypeptides with the general formula poly[Lys(Ser(i)-DL-Ala(m))], (SAK). Ser was also coupled directly to the polylysine backbone poly[Lys(Ser(i))], (S(i)K) and then elongated by polymerization of N-carboxy-DL-Ala anhydride resulting poly[Lys(DL-Ala(m)-Ser(i))], (ASK). An additional **polymer** was also prepared, but instead of the oligo(DL-Ala) **branches**, oligo(DL-Ser) side chains were introduced (poly[Lys(DL-Ser(m))], SK). The presence of hydroxyl groups resulted in compounds with improved water solubility. CD spectra of polypeptides showed significant differences correlating with the position and numbers of Ser residues in the side chains. Under physiological conditions, polycationic polypeptides assumed ordered secondary structure (S(i)K and LSK) or partially unordered conformation (SK, SAK, and ASK). Data of selected **polymers** demonstrate that these polycationic compounds are essentially nontoxic in vitro on normal rat liver or mouse spleen cells and have no cytostatic effect on mouse colorectal carcinoma C26 cells. The blood clearance and biodistribution of these derivatives were greatly dependent on the position and number of Ser residues in the **branches** and possess a rather extended blood survival in mice. Polypeptides were taken up predominantly by the liver and kidney (S(i)K, LSK, and ASK) or kidney and lung (SK and SAK). The best survival in the blood was found with SAK, representing the first polycationic branched polypeptide, which show extended blood clearance. The relative position of Ser residue had also a marked influence on the immunogenicity of polypeptides. The characteristics of the antibody response to polypeptide containing Ser at the end of the **branches** (SAK) or adjacent to the polylysine backbone (ASK) was also dependent on the genetic background of the mouse



strains. We also found that these compounds have no effect on to the SRBC-specific humoral immune response, indicating the lack of nonspecific immunostimulatory potential. In conclusion, these studies suggest that synthetic branched polypeptides with Ser can be considered as candidates for constructing suitable **conjugates** for drug/epitope delivery. It is not only due to the presence of hydroxyl group to be used for oxime chemistry but also to their beneficial biological features.

L5 ANSWER 21 OF 40 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
1999:592775 The Genuine Article (R) Number: 219QC. Bioactive surfaces via immobilization of self-assembling **polymers** onto hydrophobic materials. Bromberg L (Reprint); Salvati L. 15 SHERWOOD RD, SWAMPSCOTT, MA 01907 (Reprint); ABBOTT LABS, MEDISENSE PROD, ABBOTT PK, IL 60064. BIOCONJUGATE CHEMISTRY (JUL-AUG 1999) Vol. 10, No. 4, pp. 678-686. Publisher: AMER CHEMICAL SOC. 1155 16TH ST, NW, WASHINGTON, DC 20036. ISSN: 1043-1802. Pub. country: USA. Language: English.  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Conjugation of proteins to copolymers from poly(acrylic acid) grafted onto PEO-PPO-PEO backbone (Pluronic-PAA) following adsorption of the **conjugates** onto hydrophobic surfaces is reported. Insulin-Pluronic-PAA **conjugates** show negligible internalization of insulin into human uterine smooth muscle cells as well as enhancement of mitogenic activity. Glucose-induced release of glycated albumin complexed with a Pluronic-PAA-concanavalin **conjugate** and adsorbed onto polystyrene nanospheres may provide a model for a glucose-responsive protein delivery system or a heterogeneous diagnostic device.

L5 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN  
1997:315040 Document No. 126:293768 Selectively functionalizable dendrimers of polyoxyalkylene units. Gozzini, Luigia; Muttoni, Monica (Bracco S.P.A., Italy; Dibra S.P.A.; Gozzini, Luigia; Muttoni, Monica). PCT Int. Appl. WO 9710281 A1 19970320, 54 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-EP3934 19960909. PRIORITY: IT 1995-MI1929 19950915.

AB Branched dendrimeric macromols. of a polyvalent central nucleus connected to polyoxyalkylene dendra subunit are characterized by the presence of  $\geq 1$  **branch**, attached either directly to the core or to a dendron, which does not participate in the growth and which therefore differs from all the other functions of the macromol. The chloroalc. ClCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>OH was protected with dihydropyran to give a product named 2-(3-oxa-5-chloropentyloxy)oxane (I) and step wise reaction of I with pentaerythritol core in the presence of tetrabutylammonium bromide gave a dendrimer. The functional group of the **branch** participates in coupling or reaction with other functional compds. to **conjugate** with biol. active compds. such as lysine derivs. The dendrimers find use in drug dosage forms, compns. selective for organs and tissue, carriers for contrast agent for imaging, etc.

L5 ANSWER 23 OF 40 MEDLINE on STN DUPLICATE 6  
1998061511. PubMed ID: 9399143. Design of macromolecular biological response modifier by immobilizing of D-glucose analogue of muramyl dipeptide on carboxymethyl-dextran having mannose **branches**. Murata J; Nagae H; Ohya Y; Ouchi T. (Department of Applied Chemistry, Faculty of Engineering, Kansai University, Osaka, Japan. ) Journal of biomaterials science. Polymer edition, (1997) 8 (12) 931-46. Journal code: 9007393. ISSN: 0920-5063. Pub. country: Netherlands. Language: English.

AB It is well known that muramyl dipeptide is a minimum required structure of bacterial peptidoglycan responsible for immunoadjuvant activity. Since

mannose receptors exist on the surface of macrophages, **polymers** with branched mannose residues are expected to target moieties to macrophages. To achieve an efficient delivery of D-glucose analogue of muramyl dipeptide (GADP) via receptor-mediated endocytosis by mannose receptors on the surface of macrophages, GADP/carboxymethyl-dextran (CM-Dex)/Man **conjugate** was synthesized. Moreover, to study the effect of the introduction of mannose residues, we also synthesized GADP/CM-glucomannan (CM-GM) and GADP/CM-Dex **conjugates**. The immunological enhancement activities of their **conjugates** were evaluated by measurements of glucose consumption and beta-D-glucuronidase activity from macrophage-like cells. The GADP/CM-Dex/Man and GADP/CM-GM **conjugates** showed higher immunological enhancement activity than the GADP/CM-Dex **conjugate**. The immunological enhancement activity of GADP/CM-Dex/Man and GADP/CM-GM **conjugates** was decreased to the same level of immunological enhancement activity of GADP/CM-Dex **conjugate** under the presence of excess mannose. These results suggested that the introduction of mannose residues into GADP/CM-Dex **conjugate** could increase the affinity against macrophage and the immunological enhancement activity of GADP/CM-Dex **conjugate** itself.

L5 ANSWER 24 OF 40 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
 97:814764 The Genuine Article (R) Number: YD666. Carrier design: Synthesis and conformational studies of poly(L-lysine) based branched polypeptides with hydroxyl groups in the side chains. Mezo G; Kajtar J; Nagy I; Szekerke M; Hudecz F (Reprint). HUNGARIAN ACAD SCI, RES GRP PEPTIDE CHEM, POB 32, H-1518 BUDAPEST 112, HUNGARY (Reprint); HUNGARIAN ACAD SCI, RES GRP PEPTIDE CHEM, H-1518 BUDAPEST 112, HUNGARY; LORAND EOTVOS UNIV, INST ORGAN CHEM, H-1518 BUDAPEST 112, HUNGARY. BIOPOLYMERS (NOV 1997) Vol. 42, No. 6, pp. 719-730. Publisher: JOHN WILEY & SONS INC. 605 THIRD AVE, NEW YORK, NY 10158-0012. ISSN: 0006-3525. Pub. country: HUNGARY. Language: English.

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB In the present study the development of a new series of branched polypeptides that contain hydroxyl groups in side chains is reported. Serine or threonine were attached by 1-hydroxy-benzotriazole catalyzed active ester method to the N-terminals of oligo(DL-alanine) chains grafted to a polylysine backbone resulted in poly [Lys-(Ser(i)-DL-Ala(m))] (SAK) and poly[Lys-(Thr(i)-DL-Ala(m))] (TAK). Ser was coupled also directly to the epsilon-amino groups of polylysine followed by polymerization of N-carboxy-DL-alanine anhydride resulting oligo(DL-Ala) chain terminals. In this way a reverse sequence was built up in the side chain corresponding to the poly [Lys-(DL-Ala(m)-Ser(i))] (ASK). The number of hydroxyl groups in the **polymer** was increased by the synthesis of a branched polypeptide with oligo (DL-serine) **branches** instead of oligo(DL-alanine) ones-poly[Lys-(DL-Ser(m))] (SK). Classification of solution conformations of branched polypeptides was carried out by CD spectroscopy performed in water solution of various pH values and ionic strengths. Incorporation of single Ser residues in poly [Lys-(X-i)]-type polypeptides markedly promotes the formation of ordered structure without resulting precipitation even in high salt concentration. The presence of **branches** with multiple DL-Ser residues resulted in a slightly decreased ability of the polypeptide backbone to adopt an ordered conformation. Comparison of the CD properties of the SAK-ASK pair demonstrates that these compounds are similar showing an increased tendency to form an ordered spatial arrangement in solution at elevated pH or ionic strength; however, differences in their CD spectra suggest that SAK has higher capability to form regular conformation under comparable conditions. The replacement of Ser by the Thr residue in poly[Lys-(X-i-DL-Ala(m))] induced a conformational transition and TAK exhibited a more helical structure. These results might indicate that not only hydrophobic or ionic attraction, but also H-bond interaction, can play a role in the formation and/or stabilization of ordered conformation of branched polypeptides. Findings with the hydroxyl group containing **polymers** reported in this paper can also explain their prolonged

shelf stability and high water solubility. (C) 1997 John Wiley & Sons, Inc.

L5 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1996:171832 Document No. 124:307572 Branched synthetic peptide **conjugate** for delivery of cytotoxic moiety or diagnostic probe to cells. Gariepy, Jean (Ontario Cancer Institute, Can.). PCT Int. Appl. WO 9533766 A1 19951214, 54 pp. DESIGNATED STATES: W: CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1994-CA405 19940722. PRIORITY: US 1994-257307 19940609.

AB Branched synthetic peptide **conjugates** are disclosed which can be designated to bind to a target cell surface receptor, to penetrate into target cells, and to deliver a diagnostic probe or cytotoxic functionality to a desired site of action. The invention provides a relatively small mol. of flexible design having a branched structure for systematically incorporating a desired number of cytotoxic functions, peptide-based localization signals or diagnostic probes. The invention addresses problems associated with protein-based therapeutic or diagnostic agents. The invention provides peptide **conjugates** (D3aJ3bD2cJ2dD1eJ1f)nBPD4sJ4tD5uJ5v [a, b, c, d, e, f, s, t, u, v = 0, 1 ( $\geq 2$  of a, c, e, s, u = 1); n  $\geq 2$ ; D = peptide domain or mimic specific for binding to cell-surface receptor or for transport across cell membrane or localization in specific cell compartment, cytotoxic group, diagnostic probe; J = junctional segment or carboxyl-terminal unit which is amino acid or short peptide; BP = branched **polymer** of diaminocarboxylic acid residues; one of D1, D2, or D3 is present and is a polycationic linear peptide or peptide mimic]. A particular octopeptide of the invention contains 8 amino-terminal **branches** and 1 carboxyl-terminal arm. The **branches** are identical and composed of a linear arrangement of 3 domains: the DNA intercalator agent, acridine; a twelve-amino-acid sequence of the SV40 large T antigen that is responsible for the nuclear translocation of this protein; and a five-residue lysine repeat. The **branches** are linked to a branched **polymer** (BP) via a junctional segment of 2 glycine residues. BP is created after 3 successive couplings of L-lysine during solid-phase peptide synthesis. Preparation of octopeptides is described, as are octopeptide cytotoxicity, internalization, nuclear localization, membrane association, and endocytosis.

L5 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1995:630101 Document No. 123:27199 A nucleic acid hybridization method that amplifies the signal using probes that are **branches** attached to a **polymer** backbone. Mandrand, Bernard; Cros, Philippe; Delair, Thierry; Charles, Marie-Helene; Erout, Marie-Noelle; Pichot, Christian (Bio Merieux, Fr.). PCT Int. Appl. WO 9508000 A2 19950323, 44 pp. DESIGNATED STATES: W: CA, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (French). CODEN: PIXXD2. APPLICATION: WO 1994-FR1084 19940915. PRIORITY: FR 1993-11006 19930915.

AB A kit for the detection of a target nucleotide sequence that uses a hybridization-based amplification step to increase sensitivity is described. One of the probes is essentially a linear backbone copolymer with lateral substituents. One of these side chains is capable of hybridizing with the target sequence and the other side chains have a sequence distinct from the target or the probe but are all the same. These other side chains may also be unique to a given probe. Such a reagent enables signal amplification to be obtained, and therefore lowers the sensitivity threshold. This method may be used in tests for the detection of pathogenic organisms, or in the diagnosis of genetic diseases. The synthesis of a copolymer backbone of N-vinylpyrrolidone and N-aryloxysuccinimide and the conjugation of oligonucleotides to it is described. In test assays the use of such a probe gave a slightly lower background in controls; had a .apprx.100-fold lower threshold of detection and stronger signals above the threshold.

L5 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1995:364335 Document No. 122:158625 Synthetic carrier and immunogen.

Webber, Robert (USA). PCT Int. Appl. WO 9500540 A1 19950105, 29 pp.

DESIGNATED STATES: W: JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1994-US5981 19940526. PRIORITY: US 1993-80186 19930618.

AB A synthetic carrier for delivering at least one biol. active component to an organism utilizing a synthetically assembled peptide which may be linked to a resin. The carrier peptide includes a terminal amino acid having a pair of functional end sites, which are capable of bonding at least a pair of components including biol. active components (e.g. cytotoxin, monoclonal antibody, pharmaceutical, fatty alc., fatty acid, protein, polymeric resin, nucleotide, etc.). Further, addnl. amino acids may be attached to the branched terminal amino acid chain to form a matrix having a progressively larger number of **branches** and attachment sites. Biol. active components may be attached to the multiple **branch** chains with a high degree accuracy. Moreover, addnl. intermediate attachment sites of the matrix may be used to link other functional groups such as adjuvant peptides. The synthetic branched chain carrier may be employed to construct a synthetic immunogen of a very high purity of possessing specific coupling ratios among the various components attached to the ends of the branched chains and at other pre-defined intermediate attachment sites. Thus, specific combinations of biol. active components may be delivered by the synthetic carrier of the present invention. In example, two peptide immunogens were synthesized, coupled to a branched carrier peptide (preparation described) or conjugated with thyroglobulin, and used as immunogens to raise antibodies for immunoassay.

L5 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1996:14159 Document No. 124:202830 An efficient synthesis of

sialoglycoconjugates on a peptidase-sensitive **polymer** support.

Yamada, Kuriko; Nichimura, Shin-Ichiro (Graduate Sch. Science, Hokkaido Univ., Sapporo, 060, Japan). Tetrahedron Letters, 36(52), 9493-6

(English) 1995. CODEN: TELEAY. ISSN: 0040-4039. Publisher: Elsevier.

AB A novel method for the enzymic synthesis of oligosaccharide derivs. on a  $\alpha$ -chymotrypsin-sensitive **polymer** support is described. The primer **polymer** having N-acetyl-D-glucosamine (GlcNAc) residue linked through a phenylalanine-containing spacer moiety was successfully elongated with galactosyl and sialyltransferases to give a glycopolymer bearing sialyl  $\alpha(2 \rightarrow 6)$  N-acetylglucosamine **branches** in high yield. Subsequent hydrolysis with  $\alpha$ -chymotrypsin proceeded smoothly and afforded a versatile sialotrisaccharide derivative having a terminal amino group which can be used for creating neoglycoconjugates.

L5 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1996:149419 Document No. 124:214758 Optical phase conjugation in polyesters

with cyanoazobenzene units in the side chain. Nakagawa, Kazuo; Sato,

Moriyuki; Mukaida, Ken-ichi; Fujiwara, Hirofumi (Department Materials

Science and Engineering, Muroran Institute Technology, Hokkaido, 050,

Japan). Optical Review, 2(6), 404-2 (English) 1995. CODEN: OPREFN.

ISSN: 1340-6000. Publisher: Optical Society of Japan.

AB Efficient optical phase-**conjugate** (PC) signals in four kinds of novel polyester films containing cyanoazobenzene units in the side chain are reported. One of them can efficiently generate only the photoinduced anisotropy (PA) component of PC signal, while the other three films can simultaneously generate two types of PC signals, PA and holog. components. These **polymers** have good potential not only as a phase conjugator but also as a polarization-sensitive hologram-recording material.

L5 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1995:294200 Document No. 122:64325 Drug-delivery **polymers** and

pharmaceutical compositions employing them. Kopecek, Jindrich; Rejmanova, Pavla; Strohalm, Jiri; et al. (Ustav Makromolekulární Chemie AVCR, Czech

Rep.). Czech Rep. CZ 278551 B6 19940316, 50 pp. (Czech). CODEN: CZXXED.  
APPLICATION: CZ 1985-97 19850104.

AB Drug-delivery **polymers** can be prepared which are composed 5.0-99.7 mol% of units derived from Me-C:CH<sub>2</sub>-CO-NH-CH<sub>2</sub>-CHOH-Me, 0.2-20.0 mol% of units having the structure Me-C:CH<sub>2</sub>-CO-[NH-R-CO]-[B], where B is a bioactive mol. or drug, and 0.1-94.8 mol% of units having the structure Me-C:CH<sub>2</sub>-CO-NH-[D] or Me-C:CH<sub>2</sub>-CO-[D] or Me-C:CH<sub>2</sub>-CO-[NH-R-CO]-D, where D is a determinant and [NH-R-CO] is a spacer residue derived from Leu, Phe, Gly-Gly, Gly-Leu-Gly, Gly-Val-Ala, Gly-Phe-Ala, Gly-Leu-Phe, Gly-Leu-Ala, Ala-Val-Ala, Gly-Phe-Leu-Gly, Gly-Phe-Phe-Leu, Gly-Leu-Leu-Gly, Gly-Phe-Tyr-Ala, Gly-Phe-Gly-Phe, Ala-Gly-Val-Phe, Gly-Phe-Phe-Gly, Gly-Phe-Leu-Gly-Phe, or Gly-Gly-Phe-Leu-Gly-Phe. Copolymers containing the above components can be single or double-chained and may contain as bioactive mols. antitumor drugs, antimicrobials, parasiticides, antiinflammatories, cardiovascular agents, or nervous system agents. The determinants may be monosaccharides, disaccharides, oligosaccharides, or O-methacryloylated sugars, which are preferably linked by an amide bond to an antibody such as IgG or anti-O antibody, or a protein such as transferrin, or a hormone such as MSH. Suitable determinants are galactose, galactosamine, glucosamine, mannosamine, and fucosylamine. The peptide spacers are degradable by lysosomal enzymes, releasing the pharmacol. active agents after the copolymer is taken up by target cells. Data are presented on the antileukemic activity of several claimed copolymers against leukemia L1210, and antitumor activity against melanoma and human hepatoma.

L5 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1994:264827 Document No. 120:264827 Metal chelating peptide. Gariepy, Jean (Ontario Cancer Institute, Can.). PCT Int. Appl. WO 9323425 A1 19931125, 25 pp. DESIGNATED STATES: W: JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1993-CA207 19930507. PRIORITY: US 1992-880691 19920508.

AB A branched peptide carrying a number of chelating groups (metal chelating peptide (MCP)) has a C-terminus that may be structured to provide a variety of means for unidirectional coupling to a targeting agent such as an antibody. The number of metal chelating sites may be quite large (in excess of 16). The MCP can be used to deliver a concentrated radionuclide mass to a target cell by coupling the MCP to a targeting agent. A branched peptide with a C-terminal  $\beta$ -alanine was synthesized by t-Boc chemical with **branches** introduced by coupling to  $\epsilon$ -amino groups of lysine and EDTA moieties added as the t-Bu protected derivative. Methods for coupling the protein to antibodies via the carbohydrate moiety using a maleimide are discussed.

L5 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1994:27026 Document No. 120:27026 Encoded combinatorial chemical libraries. Lerner, Richard; Janda, Kim; Brenner, Sydney; Nielsen, John (Scripps Research Institute, USA). PCT Int. Appl. WO 9320242 A1 19931014, 96 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US3127 19930330. PRIORITY: US 1992-860445 19920330.

AB A method of screening synthetic compds. (e.g. series of peptides) for biol. (binding, activating, catalytic, etc.) activity involves synthesis of a library of bifunctional mols., each comprising a candidate active **polymer** and an identifying synthetic genetic tag. Two alternating parallel combinatorial syntheses are performed, such that addition of 1 chemical

unit to the candidate active compound is followed by addition of an identifying oligonucleotide sequence; the library is built up by repetition of this process. Serial enrichment of active mols. is achieved by PCR amplification of and hybridization with their genetic tag sequences; sequencing the genetic tag identifies the sequence of the active mol. Thus, activated controlled-pore glass was coupled in 2 steps with an aqueous NH<sub>3</sub>-cleavable sarcosine-succinyl-6-aminohexanol linker, and a bifunctional **branch** monomer, O-(4,4'-dimethoxytrityl)-N-

fluorenylmethoxycarbonylserine, was added by amidation of the terminal amino group of aminohexanol. Removal of the dimethoxytrityl group allowed addition of a blocked nucleotide phosphoramidite, and subsequent removal of the fluorenylmethoxycarbonyl group allowed addition of a protected amino acid; addnl. nucleotide and amino acid residues were added alternately. The synthesis included the steps of aliquoting, adding different units to each aliquot, and pooling the aliquots to build the library of bifunctional mols. sequentially. PCR primer binding sites may be added as blocks rather than added nucleotide by nucleotide.

L5 ANSWER 33 OF 40 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 7

1993:188870 Document No.: PREV199395099320. Influence of carrier on biodistribution and in vitro cytotoxicity of methotrexate-branched polypeptide **conjugates**. Hudecz, F. [Reprint author]; Clegg, J. A.; Kajtar, J.; Embleton, M. J.; Pimm, M. V.; Szekerke, M.; Baldwin, R. W.. Res. Group Peptide Chem., Hung. Acad. Sci., P.O. Box 32, Budapest 112, H-1518 Hung, hungary. Bioconjugate Chemistry, (1993) Vol. 4, No. 1, pp. 25-33.

CODEN: BCCHES. ISSN: 1043-1802. Language: English.

AB Methotrexate (MTX) has been conjugated to various structurally related, synthetic, branched polypeptides containing a poly(L-Lys) backbone by the aid of water-soluble carbodiimide. The average degree of MTX incorporated was found to be dependent on the size of the **polymer** and on the identity of the terminal amino acid residue of the side chains. Consequently the average molar substitution ratio was the range of 4.9-7.2 MTX per carrier molecule. CD spectra of **conjugates** showed significant differences in solution conformation correlating with the identity of the side-chain-terminating amino acid. Polycationic **conjugates** XAK-MTX (X = Leu or D-Leu) assumed essentially ordered (helical) secondary structure, while the CD spectrum of the amphoteric **conjugate** (X = Glu) corresponded to only a partially ordered conformation in PBS. The covalent attachment of MTX to branched polypeptides results in a reduction of drug in vitro cytotoxicity influenced by the carrier structure. Conjugation to amphoteric polymerse, depending on the configuration and position of glutamic acid (XAK-MTX vs AXK-MTX type **conjugates**) resulted in a decrease of anti-791T cell activity. However polycationic **conjugates** bearing L-Leu at the side chain terminal position (LAK-MTX) produced a compound with cytotoxicity only about 60 times less effective than free MTX. The biodistribution in mice has been characterized by blood clearance, whole-body retention, and tissue distribution 24 h after iv administration. Blood clearance of MTX-branched polypeptides could be significantly prolonged by incorporation of glutamic acid into the side chain. The presence of a D-amino acid in the terminal position of the side chain (D-LAK-MTX vs LAK-MTX) or adjacent to the polylysine backbone (a-D-ek-MTX vs aek-MTX) resulted in an elevated whole-body survival. Interestingly enough, the retarded blood survival of amphoteric or polycationic **conjugates** did not implicate similar tissue distribution. Polycationic carriers were directed predominantly to spleen, liver, and kidney, while **conjugates** with Glu in the side chain were taken up by the lung, kidney, and liver. It was demonstrated that branched polypeptide-MTX **conjugates** constructed from a polycationic or even amphoteric carrier can (a) sustain the cytotoxic activity of MTX at a level comparable to that of the frequently used HSA-MTX and (b) be present in the circulation (amphoteric **conjugates**) and/or in the body (both amphoteric and polycationic **conjugates**) for a much longer period of time than HSA-MTX or free drug. This study suggests that it is feasible to alter beneficially the body distribution and in vitro toxicity of MTX by logical combination of side-chain sequence, configuration, and identity of amino acid X in the **branches** of the carrier molecule.

L5 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN  
1993:61436 Document No. 118:61436 Synthetic **conjugate** fibers spun

from polyurethanes and polyesters with improved dyeing leveling. Maeda, Yoshinuki; Yokota, Nobuhiko; Uehata, Akihiro; Saito, Tadashi (Kuraray Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 04185715 A2 19920702 Heisei, 5 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1990-304864 19901109.

AB The title fibers consist of polyurethanes containing OR10COR2CO units (R1 = C6-10 alkylene groups containing 1 Me **branch**; R2 = divalent organic group) and polyesters. Thus, azelaic acid-1,4-butanediol-MDI-3-methyl-1,5-pentanediol copolymer (I) and PET were together melt spun and drawn. Leveling was good in dyeing a knit of this fiber with a liquid containing 3% (on fiber) Sumikaron Orange SE-RPD for 30 min at 125°. Leveling was poor for a knit prepared using a polyurethane containing polytetramethylene glycol segments instead of I.

L5 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1991:165565 Document No. 114:165565 Crack propagation in brittle materials under compressive stresses studied by caustics. Theocaris, P. S.; Sakellariou, M. (Dep. Eng. Sci., Athens Natl. Tech. Univ., Athens, 17510, Greece). Journal of Materials Science, 26(6), 1640-6 (English) 1991. CODEN: JMTSAS. ISSN: 0022-2461.

AB Using the equations of the deformed shape of a crack and by introducing a correction model to prevent the crack lips from incompatible displacements, the stress distribution along the crack borders was estimated. An opening-mode stress intensity factor must be introduced at the crack tips in the overall compressive stress field to give the required space for the lip-slip phenomenon, due to shearing, to occur. This local dilatation in the vicinity of the crack tip, together with the lip-slip phenomenon, due to which the initial crack tip is displaced to a new position along the deformed crack borders, causes out-of-plane propagation of the crack, either towards the largest compressive stress in the case of biaxial stress field, or towards the applied compression in a uniaxial compressive field. A series of expts. on PMMA rectangular specimens with pre-existing cracks and slits was executed and the type of the stress field in the front of the propagated **branches** is examined using the method of caustics. Crack propagation under compression is an interactive process of 2 **conjugate branches**, which is strongly influenced by the boundary conditions of the pre-existed discontinuity.

L5 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1991:602731 Document No. 115:202731 Improved amplified nucleic acid hybridization assays for hepatitis B virus (HBV), and synthesis of linear and branched oligonucleotide multimers therefor. Urdea, Michael S.; Warner, Brian; Running, Joyce A.; Kolberg, Janice A.; Clyne, Jennifer M.; Sanchez-Pescador, Ray; Horn, Thomas (Chiron Corp., USA). PCT Int. Appl. WO 9013667 A1 19901115, 73 pp. DESIGNATED STATES: W: AU, JP, KR; RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1990-US2049 19900416. PRIORITY: US 1989-340031 19890418.

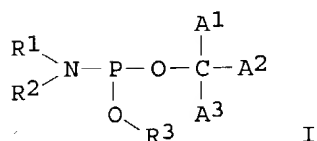
AB Amplified, solution-phase sandwich nucleic acid hybridization assays for HBV are provided in which (1) analyte is hybridized in solution with sets of amplifier probe oligonucleotides and capture probe oligonucleotides, each having (a) a 1st segment that is complementary to a consensus HBV double strand region sequence based on a multiplicity of HBV subtypes and (b) a 2nd segment that is complementary to a unit of an oligonucleotide multimer and an oligonucleotide bound to a solid phase, resp.; (2) the resulting product is reacted with the oligonucleotide bound to the solid phase; (3) the resulting product is washed to remove unbound materials; (4) the bound materials are reacted with the multimer; (5) the bound materials are washed to remove unbound multimer; and (6) the bound materials are reacted with a labeled probe complementary to the oligonucleotide units of the multimer. Preparation of linear and branched multimers, of phosphoramidites for forming comb-like points, of a multifunctional phosphoramidite for forming bifurcated **branch** points, etc. are described. In an assay for ABV in serum using e.g. a chemical crosslinked, branched multimer preparation, the signal/noise ratio was 9.9.

L5 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN  
 1991:35994 Document No. 114:35994 Multiple-unit **polymer**-bound  
 peptidyl carbamate inhibitors for inflammation-associated elastase.  
 Digenis, George A.; Banks, William R.; Rypacek, Frantisek; Agha, Bushra  
 (University of Kentucky Research Foundation, USA; Czechoslovak Academy of  
 Sciences). PCT Int. Appl. WO 9002558 A1 19900322, 54 pp. DESIGNATED  
 STATES: W: AU, JP; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE.  
 (English). CODEN: PIXXD2. APPLICATION: WO 1989-US3908 19890908.  
 PRIORITY: US 1988-242294 19880909.

AB The title polymeric elastase inhibitors comprise P(LR)q [I; P =  
 nonbiodegradable **polymer** AmBn (A, B = monomers; m, n = 5-3000);  
 L = covalent bond, linker group; R = O-succinyl-Ala-Ala-Pro-  
 CH<sub>2</sub>N(R<sub>1</sub>)C(O)XR<sub>2</sub> (X = O, S; R<sub>1</sub> = unbonded or secondary-**branch** C1-4  
 alkyl, C2-3 alkenyl, C2-4 alkynyl, C3-6 cycloalkyl, PhCH<sub>2</sub>; R<sub>2</sub> =  
 (un)substituted Ph (with provisions); q = 1 to m+n]. I have higher biol.  
 half-life and/or potency with respect to elastase inhibition. Thus,  
 p-nitrophenyl-N-(succinyl-L-Ala-L-Ala-L-prolylmethyl)-N-iso-Pr carbamate  
 (II) was prepared in 3 steps from t-Boc-L-alanyl-L-alanine (preparation given)  
 (Boc = tert-butoxy carbonyl). A **polymer** carrier mol. was prepared  
 by reacting polysuccinimide with mono-N-Boc-1,2-diaminoethane benzoate and  
 reacting the product with CF<sub>3</sub>CO<sub>2</sub>H. II was then reacted with the prepared  
**polymer** to give a **polymer**-bound inhibitor, which was  
 characterized. A **polymer**-bound peptidyl carbamate inhibitor of  
 the invention resulted in ≥700-fold decrease in K<sub>i</sub> (inhibition  
 constant) with respect to elastase inhibition. Even if the **polymer**-  
 bound peptidyl carbamate inhibitor contained as low as 1.6 mol% peptidyl  
 carbamate units, it would, in the assay used, be at least as active as  
 α1-proteinase inhibitor.

L5 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN  
 1990:512021 Document No. 113:112021 Preparation of oligonucleotide  
 hybridization probes and a reagent useful in the preparation.  
 Kwiatkowski, Marek; Sund, Christian; Hurskainen, Pertti (Wallac Oy,  
 Finland; Pharmacia AB). PCT Int. Appl. WO 9000622 A1 19900125, 48 pp.  
 DESIGNATED STATES: W: JP, US; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE.  
 (English). CODEN: PIXXD2. APPLICATION: WO 1989-SE377 19890703.  
 PRIORITY: SE 1988-2574 19880708.

GI



AB The title probes comprise a sequence of 16-200 nucleotides labeled at 1 of  
 the terminal positions with a branched **polymer** containing >1  
 neg.-charged groups, preferably phosphodiester groups, and optionally >1  
 anal. detectable groups, e.g. lanthanide chelates, covalently bonded to  
 the terminal ends of the **branches** of the **polymers**.  
 The branched **polymer** contains an amplified number of reactive  
 hydroxyl groups to which the detectable groups can be attached and allows  
 the opportunity of many detectable groups in each probe oligonucleotide  
 chain. The probe of the invention is prepared by multiple rounds of  
 coupling of I [R<sub>1</sub>, R<sub>2</sub> = lower alkyl; R<sub>3</sub> = (un)substituted C1-7 alkyl,  
 (un)substituted aryl; A<sub>1</sub>-A<sub>3</sub> = H, A'OB, A''OB, A'''OB (B = protecting  
 group; A', A'', A''' = hydrocarbon chain providing 5-9 atom distance  
 between P and O directly bonded to B; at most 1 of A<sub>1</sub>-A<sub>3</sub> = H)] to the  
 oligonucleotide terminus. Thus, 1,7-di-O-(4,4'-dimethoxytrityl)heptane  
 4-(N,N-diisopropylamino)cianoethylphosphoramidite was prepared from reaction  
 of (N,N-diisopropylamino)cianoethylphosphoramidic chloride with



1,7-di-O-(4,4'-dimethoxytrityl)-4-hydroxyheptane in presence of N,N-diisopropylethylamine (preparation given). A probe was constructed from a 50-mer synthetic oligonucleotide having a sequence complementary to  $\lambda$ -phage DNA by couplings of the OH-amplifying reagent, followed by labeling of the OH-amplified products with a phosphoramido form of a europium chelate moiety. A detection limit of 400 pg  $\lambda$ -phage DNA was obtained in a hybridization assay using the prepared probe.

L5 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1990:194916 Document No. 112:194916 Nucleic acid multimers and amplified nucleic acid hybridization assays and immunoassays using the multimers. Urdea, Michael S.; Warner, Brian; Running, Joyce A.; Kolberg, Janice A.; Clyne, Jennifer M.; Sanchez-Pescador, Ray; Horn, Thomas (Chiron Corp., USA). PCT Int. Appl. WO 8903891 A1 19890505, 112 pp. DESIGNATED STATES: W: DK. (English). CODEN: PIXXD2. APPLICATION: WO 1988-US3644 19881014. PRIORITY: US 1987-109282 19871015; US 1988-185201 19880422; US 1988-252638 19880930.

AB Linear or branched oligonucleotide multimers useful as amplifiers in biochem. assays are prepared comprising  $\geq 1$  1st single-stranded oligonucleotide unit that is complementary to a single-stranded oligonucleotide sequence of interest and a multiplicity of 2nd single-stranded oligonucleotide units that are complementary to a single-stranded labeled oligonucleotide. Amplified (sandwich) nucleic acid hybridization assays and immunoassays using the multimers are exemplified as well as capture and amplifier probes useful in these assays. A sandwich hybridization assay for *Neisseria gonorrhoeae* DNA used probes based on *N. gonorrhoeae* genomic sequence SSJK1. Capture and amplification 50-mer probes comprised 30 nucleotides complementary to regions of SSJK1 in their 5' end and either the sequence CTTCTTTGGAGAAAGTGGTG (I) or TTAGGCATAGGACCCGTGTC (II), resp., at the 3' end. A 21-mer complementary to I was immobilized in microtiter wells. An amplification multimer comprising a 5-site comb structure had **branches** complementary to II and to an oligonucleotide labeled with alkaline phosphatase or horseradish peroxidase. Crude cellular lysates and genomic DNA from different bacteria were assayed. Only *N. gonorrhoeae* samples (17 strains representing various serotypes) were pos. with signal-to-noise ratios  $> 3$ . A 4-site comb amplification multimer was synthesized by treating (TTO)3TTGACACGGGTCTATGCCT [O = 5'-dimethoxytrityl-N4-(O-levulinyl)hexamethylene]-5-methylcytidine Me phosphoramidite] with hydrazine in pyridine/HOAc (8:2) to remove the O-levulinyl group, synthesizing an 18-mer complementary to II off the 5' end and at each O residue, deprotecting, etc.

L5 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN

1987:435781 Document No. 107:35781 Magnetic resonance imaging of gadolinium-labeled monoclonal antibody **polymers** directed at human T lymphocytes implanted in canine brain. Kornguth, Steven E.; Turski, Patrick A.; Perman, William H.; Schultz, Ronald; Kalinke, Tom; Reale, Richard; Raybaud, Francois (Med. Sch., Univ. Wisconsin, Madison, WI, USA). Journal of Neurosurgery, 66(6), 898-906 (English) 1987. CODEN: JONSAC. ISSN: 0022-3085.

AB Two different murine monoclonal anti-human T cell antibodies that were coupled to Gd bind specifically to human T lymphocytes cells implanted in canine brain. This binding was at a concentration of Gd sufficient to detect

the implanted cells and to distinguish them from the surrounding brain tissue with magnetic resonance imaging (MRI) at a field strength of 1.5 T. These Gd-labeled Ig preps. did not bind bovine T cells at a concns. sufficient to be detected on MRI. A protein solution containing the Igs (100  $\mu$ g), gelatin (2 mg), and bovine serum albumin (2.5 mg) was reacted with the dianhydride of DTPA; the DTPA serves as a metal chelator and as a protein crosslinking agent. The DTPA-protein complex was reacted with GdCl<sub>2</sub>. There were .apprx.10 DTPA residues per protein mol. in the modified protein mixture Isolated human or bovine monocytes (.apprx.12 million cells) were implanted in the brains of anesthetized dogs in a volume of 40

$\mu$ L. The blood-brain barrier was then disrupted by the intra-arterial injection of hyperosmotic mannitol, and the Gd-labeled antibodies were injected through a catheter placed at the **branch** of the internal and external carotid arteries. The brains were imaged 48-72 h later. The MRI scans revealed a markedly decreased T1 relaxation time with a high signal intensity related to the human T cells implants. There was no evidence of decreased T1 at the site of the bovine T cells. Neither control murine globulin Gd-DTPA nor anti-human T cell antibodies uncoupled to Gd modified the MRI contrast of the human T cells in the brain.

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(FILE 'HOME' ENTERED AT 10:24:51 ON 01 JUN 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 10:25:01 ON 01 JUN 2004

L1 230847 S CONJUGATE  
L2 1 S L1 AND BRANCHING GROUPS  
L3 11373 S L1 AND POLYMER  
L4 60 S L3 AND BRANCH  
L5 40 DUP REMOVE L4 (20 DUPLICATES REMOVED)

=> s l1 and polyethylene glycol

L6 3691 L1 AND POLYETHYLENE GLYCOL

=> s l6 and triethylene glycol

L7 20 L6 AND TRIETHYLENE GLYCOL

=> dup remove l7

PROCESSING COMPLETED FOR L7

L8 19 DUP REMOVE L7 (1 DUPLICATE REMOVED)

=> d l8 1-19 cbib abs

L8 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

2004:162445 Document No. 140:193075 Pharmaceutical compositions of insulin drug-oligomer **conjugates** and methods of treating diseases therewith. Soltero, Richard; Radhakrishnan, Balasingam; Ekwuribe, Nnochiri N.; Rehlaender, Bruce; Hickey, Anthony; Bovet, Li Li (USA). U.S. Pat. Appl. Publ. US 2004038866 A1 20040226, 40 pp., Cont.-in-part of U.S. Ser. No. 235,284. (English). CODEN: USXXCO. APPLICATION: US 2003-382155 20030305. PRIORITY: US 2001-PV318193 20010907; US 2002-PV377865 20020503; US 2002-235284 20020905; US 2002-235281 20020905.

AB Pharmaceutical compns. that include insulin, an insulin drug-oligomer **conjugate**, a fatty acid component, and a bile salt component or a bile salt component without a fatty acid component are described. The insulin drug is covalently coupled to an oligomeric moiety. The fatty acid component and the bile salt component, when together, can be present in a weight-to-weight ratio of between 1:15 and 15:1. Methods of treating an insulin deficiency in a subject in need of such treatment using such pharmaceutical compns. are also provided, as are methods of providing such pharmaceutical compns. Substantial redns. in blood glucose were observed as the result of coadministration of hexyl-insulin monoconjugate 2 (HIM2) and bile salts to mice and dogs. All of the bile salts were effective at a level of 1.5 %.

L8 ANSWER 2 OF 19 MEDLINE on STN

2004083591. PubMed ID: 14971899. Design, synthesis, and biological evaluation of doxorubicin-formaldehyde **conjugates** targeted to breast cancer cells. Burke Patrick J; Koch Tad H. (Department of Chemistry and Biochemistry, University of Colorado, Boulder, Colorado 80309-0215, USA. ) Journal of medicinal chemistry, (2004 Feb 26) 47 (5) 1193-206. Journal code: 9716531. ISSN: 0022-2623. Pub. country: United States. Language: English.

AB The anthracycline antitumor drug doxorubicin (DOX) has been utilized for decades as a broad-spectrum chemotherapeutic. Recent literature evidence documents the role of formaldehyde in the cytotoxic mechanism, and anthracycline-formaldehyde **conjugates** possess substantially enhanced activity in vitro and in vivo. Targeting a doxorubicin-formaldehyde **conjugate** specifically to cancer cells may provide a more efficacious chemotherapeutic. The design and 11-step synthesis of doxorubicin-formaldehyde **conjugates** targeted to the estrogen receptor, which is commonly overexpressed in breast cancer cells, are reported. The formaldehyde is incorporated in a masked form as an N-Mannich linkage between doxorubicin and salicylamide. The salicylamide triggering molecule, previously developed to release the doxorubicin-formaldehyde active metabolite, is tethered via derivatized ethylene glycols to an E and Z mixture of 4-hydroxytamoxifen. The targeting group, E/Z-4-hydroxytamoxifen, was selected for its ability to tightly bind the estrogen receptor and antiestrogen binding sites. The targeted doxorubicin-formaldehyde **conjugates'** estrogen receptor binding and in vitro growth inhibition were evaluated as a function of tether length. The lead compound, DOX-TEG-TAM, bearing a **triethylene glycol** tether, binds the estrogen receptor with a binding affinity of 2.5% relative to E/Z-4-hydroxytamoxifen and inhibits the growth of four breast cancer cell lines with 4-fold up to 140-fold enhanced activity relative to doxorubicin.

L8 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN  
2003:221462 Document No. 138:260437 Pharmaceutical compositions of drug-oligomer **conjugates** for oral administration. Soltero, Richard; Ekwuribe, Nnochiri N.; Opawale, Foyeke; Rehlaender, Bruce; Hickey, Anthony; Bovet, Li Li (Nobex Corporation, USA). PCT Int. Appl. WO 2003022210 A2 20030320, 96 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US28536 20020906. PRIORITY: US 2001-PV318193 20010907; US 2002-PV377865 20020503.

AB An oral pharmaceutical composition comprising a drug-oligomer **conjugate**, 0.1-15% of a fatty acid component, and 0.1-15% of a bile salt component is described. The drug, e.g., a peptide or protein, is covalently coupled to an oligomeric moiety. The fatty acid component and the bile salt component are present in a weight-to-weight ratio of between 1:5 and 5:1. Methods of treating diseases in a subject in need of such treatment using such pharmaceutical compns. are also provided, as are methods of providing such pharmaceutical compns. For example, tablets containing an insulin **conjugate** HIM2 were prepared by lyophilization of a mixture containing HIM2 2.5 g, Na cholate 30.0 g, oleic acid 10.0 g, 25% sucralose 8.0 g, flavor 4.0 g, capric acid 5.0 g, lauric acid 5.0 g, citric acid 67.2 g, trolamine 42.4 g, NaOH 18.8 g, pH adjusters (5N NaOH and 5N HCl) as needed, and water resulting in an amorphous powder. The powder (127.6 g) was blended with citric acid 29.7 g, sodium citrate 84.2 g, Tris base 106.7 g, microcryst. cellulose 24.8 g, and Explotab 9.4 g and compressed into tablets.

L8 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN  
2003:609944 Document No. 139:160746 Methods for detection and quantitation of nucleic acids for diagnosis of genetic diseases and infections and forensic, food and environmental screening. Vision, Todd J.; Carmon, Amber; Thannhauser, Theodore W.; Kresovich, Stephen; Mitchell, Sharon E.; Muller, Uwe R. (USA). U.S. Pat. Appl. Publ. US 2003148284 A1 20030807, 24 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-23337 20011217.

AB Methods for detection and quantitation of nucleic acids for diagnosis of genetic diseases and infections as well as forensic, food, feed and

environmental screening are provided. An immobilized oligonucleotide primer is extended using a polymerase, yielding an extension product that can be used in a detection assay. The assay is useful for detecting the presence of a target nucleic acid mol. in a sample and quantifying the amount of the target nucleic acid mol. in the sample.

L8 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

2002:946134 Document No. 138:16636 Preparation of calcitonin drug-alkylene glycol oligomer **conjugates**. Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L. (Nobex Corporation, USA). PCT Int. Appl. WO 2002098451 A1 20021212, 126 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17575 20020604. PRIORITY: US 2001-873777 20010604.

AB A mixture of **conjugates** in which each **conjugate** in the mixture comprises a calcitonin drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixture may lower serum calcium levels in a subject by 10, 15 or  $\geq 20\%$ . Moreover, the mixture may be more effective at surviving an in vitro model of intestinal digestion than non-conjugated calcitonin. Furthermore, the mixture may exhibit a higher bioavailability than the non-conjugated calcitonin. Thus, non-polydispersed hexaethylene glycol was treated with phosgene solution, followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Salmon calcitonin was allowed to react with the NHS ester to give the **conjugate**.

L8 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

2002:946130 Document No. 138:29120 Preparation of peptide drug-alkylene glycol oligomer **conjugates**. Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L. (Nobex Corporation, USA). PCT Int. Appl. WO 2002098446 A1 20021212, 201 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US17567 20020604. PRIORITY: US 2001-873797 20010604.

AB A non-polydispersed mixture of **conjugates** in which each **conjugate** in the mixture comprises a peptide drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixture may exhibit higher in vivo activity than a polydispersed mixture of similar **conjugates**. The mixture may be more effective at surviving an in vitro model of intestinal digestion than polydispersed mixts. of similar **conjugates**. The mixture may result in less inter-subject variability than polydispersed mixts. of similar **conjugates**. Thus, non-polydispersed hexaethylene glycol was treated with phosgene solution, followed by treatment with N-hydroxysuccinimide (NHS) to give the NHS ester. Human growth hormone (Saizen) was allowed to react with the NHS ester to give the **conjugate**.

L8 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

2002:185224 Document No. 136:232720 Degradable polyacetal polymers. Brocchini, Stephen; Heller, Jorge; Tomlinson, Ryan; Duncan, Ruth; Garrett, Shane; Klee, Marcus (Ap Pharma, Inc., USA). PCT Int. Appl. WO 2002020663 A2 20020314, 55 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ,

BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US27664 20010906.

PRIORITY: US 2000-PV230377 20000906.

- AB Degradable polyacetal polymers and functionalized degradable polyacetal polymers have properties favorable for use in pharmaceutical and biomedical applications. The degradable polyacetal polymers are relatively stable at physiolo. pH with favorable biodistribution profiles, and degrade readily in low pH conditions. **Conjugates** of the polymers with drugs, especially anticancer drugs, and use for treatment of cancer. These polyacetals are manufactured by polymerization of diols having hydrocarbon chains optionally containing  $\geq 1$  O bridge such as PEG and divinyl ethers of compds. containing a group capable of being covalently conjugated with a bioactive agent via peptidic or a hydrolytically-labile bond. A typical polyacetal was manufactured by heating 17 g PEG

(number-average mol.

weight 3400), 0.03 g toluenesulfonic acid monohydrate, and 60 mL PhMe 2 h at 150°, cooling to 50°, adding 1.073 g **triethylene glycol** divinyl ether and 30 mL PhMe, and stirring 2 h at room temperature

- L8 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN  
2001:185606 Document No. 134:227429 Enzyme inhibitors for use in preventing skin irritation in absorbent articles. Osborne, Scott Edward; Underiner, Todd Laurence (Procter & Gamble Co., USA). PCT Int. Appl. WO 2001017565 A2 20010315, 59 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US24712 20000908. PRIORITY: US 1999-PV153418 19990910.

- AB The present invention relates to compns. which comprise one or more polymer **conjugates** having the formula poly(LaT)<sub>i</sub> wherein T is a heterocyclic unit which is capable of inhibiting one or more proteolytic enzymes; L is a linking group; [Poly] is a polymeric unit, i indicates the number of said heterocyclic units which comprise said **conjugate** and has the value of from 1 to 100; a is 0 or 1, said polymer **conjugates** suitable for use in preventing skin irritation resulting from exposure of the skin to body fluids, inter alia, faces, menstrual fluid. The **conjugates** of the present invention are useful in diapers, dressings, sanitary napkins, and the like. Methyl-2-isocyanatobenzoate was reacted with PEG-5000 amine to obtain PEG-5000 urea which was separated PEG-5000 urea was treated with concentrated sulfuric acid, excess acid was neutralized with sodium bicarbonate and extracted with dichloromethane to obtain 4H-benzoxazin-4-one linked by an N-ethylene-N'-phenylene urea moiety to a **polyethylene glycol** polymer comprising an average mol. weight about 5000 dalton. Efficacy of the polymer **conjugate** of the invention in inhibition of interleukin 1 $\alpha$  is shown. Formulation of a composition for an absorbent article containing 10% of the polymer **conjugate** of the invention is disclosed.

- L8 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN  
2001:224355 Document No. 134:265135 B-cell tolerogens for treatment for pathologies mediated by antibodies to phospholipids. Victoria, Edward Jess; Marquis, David Matthew; Jones, David S.; Yu, Lin (La Jolla

Pharmaceutical Company, USA). U.S. US 6207160 B1 20010327, 113 pp., Cont.-in-part of U.S. 5,874,409. (English). CODEN: USXXAM. APPLICATION: US 1996-660092 19960606. PRIORITY: US 1995-482651 19950607.

AB The authors disclose analogs of anti-phospholipid antibody (aPL) epitopes that (a) bind specifically to B cells to and (b) do not induce T-cell activation. In addition, the authors disclose the preparation of non-immunogenic tetraivalent scaffolds to which the synthetic tolerogens can be attached.

L8 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

2000:911065 Document No. 134:76386 Amphiphilic drug-oligomer **conjugates** with hydrolyzable lipophile components and methods for making and using the same. Ekwuribe, Nnochiri; Ramaswamy, Muthukumar; Rajagopalan, Jayanthi (Protein Delivery, Inc., USA). PCT Int. Appl. WO 2000078302 A1 20001228, 69 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US16879 20000619. PRIORITY: US 1999-336548 19990619.

AB The present invention relates generally to hydrolyzable drug-oligomer **conjugates**, pharmaceutical compns. comprising such **conjugates**, and to methods for making and using such **conjugates** and pharmaceutical compns. For example, a **conjugate** of insulin, PEG, and oleic acid was prepared and can be orally administered.

L8 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

2000:307077 Document No. 132:320935 Induction of humoral anergy using immunogen **conjugates** lacking T-cell epitopes. Coutts, Stephen M.; Barstad, Paul A.; Iverson, G. Michael; Jones, David S. (La Jolla Pharmaceutical Company, USA). U.S. US 6060056 A 20000509, 30 pp., Cont.-in-part of U.S. 5,268,454. (English). CODEN: USXXAM. APPLICATION: US 1993-118055 19930908. PRIORITY: US 1991-652648 19910208.

AB The authors disclose the preparation of **conjugates** of non-immunogenic carrier mols. with B-cell epitopes that possess ability to suppress antigen-specific antibody responses. In one example, mice were primed with the main immunogenic region of the acetylcholine receptor. Subsequent immunization of these mice with a B-cell epitope peptide, lacking the ability to activate primed T-cells, led to a specific suppression of the anti-receptor antibody response. In a second example, mice were primed with the bee venom allergen, mellitin. Immunization with peptides conjugated to lysine-glutamate copolymer suppressed the anti-mellitin response.

L8 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

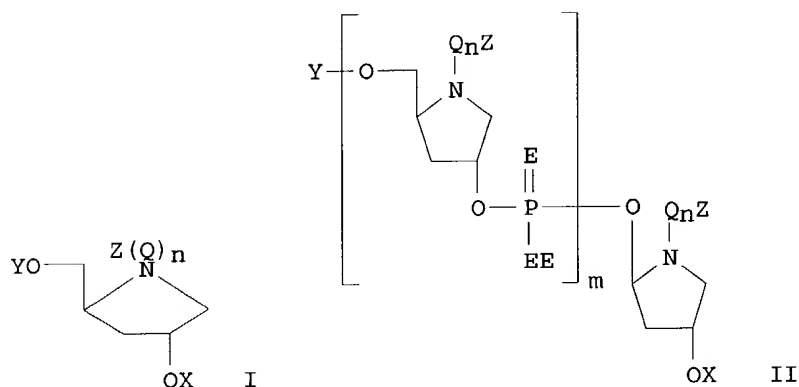
2000:155284 Document No. 132:299366 Equilibrium Swelling Behavior of Solid Supported Poly(ethylene glycol) Lipid Monolayers. Effects of Short Chain Lengths. Mathe, Gerald; Gege, Christian; Neumaier, Klaus R.; Schmidt, Richard R.; Sackmann, Erich (Physik-Department, Technischen Universitaet Muenchen, Garching, 85748, Germany). Langmuir, 16(8), 3835-3845 (English) 2000. CODEN: LANGD5. ISSN: 0743-7463. Publisher: American Chemical Society.

AB Phase transitions and thermodyn. properties of monolayers of short poly(ethylene glycol) chains (abbreviated as EG) covalently attached to lipids were determined by analyzing pressure-area isotherms at 3 different temps. by using a film balance. The EG chain lengths were varied systematically between  $N = 3$  and  $N = 15$  repeating EG units. For the 2 longest EG chains ( $N = 12$  and  $N = 15$ ) a new synthesis is described. For short chains ( $N < 9$ ) the monolayer phase transition is determined by the alkyl chain moiety of the headgroup, while for  $N \geq 9$  the typical behavior of lipopolymers is observed. For the fluid-gel phase transition the entropy

and the corresponding latent heat were determined for 3, 6, and 9 EG lipids. In the 2nd part the lipids were transferred to hydrophilic Si oxide substrates by the Langmuir-Blodgett technique and characterized by their equilibrium swelling behavior under controlled humidity by using ellipsometry. In agreement with the monolayer expts., the authors find a polymer brush-like behavior already at chain lengths of  $N \geq 12$  despite the fact that the statistical limit  $N \gg 1$  is hardly fulfilled. For ds.p. of  $N = 3$  and  $N = 6$  EG units, relative small swelling ratios  $\rho$  are observed due to a rigid rod-like behavior. Between  $N = 6$  and  $N = 9$  repeating units an intermediate swelling behavior is found.

L8 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN  
 1995:986305 Document No. 124:30274 Preparation of pyrrolidine-containing monomers and oligomers.. Acevedo, Oscar L.; Hebert, Normand (Isis Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 9518792 A1 19950713, 96 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2.  
 APPLICATION: WO 1995-US356 19950111. PRIORITY: US 1994-180134 19940111.

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AB Monomers (I; X = H, phosphate, activated phosphate, activated phosphite, solid support; Y = H, protecting group; Z = L1, L1G1, L2G2, NR3R4, N-heterocyclyl, purinyl, pyrimidinyl, phosphate, polyether residue, **polyethylene glycol** residue; L1 = alkyl, alkenyl, alkynyl; L2 = aryl, aralkyl; G1 = halo, OR1, SR2, NR3R4, CHO, CONR3R4, etc.; R1-R4 = H, alkyl, protecting group; Q = L1, G3, L1G3, G3L1G3; G3 = CO, CS, CO2, CONH, CSO, CSNH, SO2; n = 0, 1), and oligomers [II; X = H, phosphate, activated phosphate, activated phosphite, solid support, **conjugate** group, oligonucleotide residue; Y = H, protecting group, **conjugate** group, oligonucleotide residue; E = O, S; EE = O-, NYT; Y = H, (Q2)jZ2; T = (Q1)kZ1; YT = atoms to form a heterocycle; Q1, Q2 = alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aralkyl, polyalkylglycol residue, etc.; j, k = 0, 1; Z1, Z2 = H, alkyl, alkenyl, alkynyl, aryl, aralkyl, halo, CHO, OR1, SR2, NR3R4, CONR3R4, reporter group, metal coordination group, N-heterocyclyl, etc; m = 1-50; n = 0, 1; Q = alkyl, acyl, CO2, CSO, CSNH, SO2, etc.; Z = alkyl, alkenyl, alkynyl, aryl, OR1, SR2, CONR3R4, OH, SH, SMe, phosphate, metal coordination group, etc.], were prepared Oligomer libraries were prepared and found to inhibit phospholipase A2 and leukotriene B4 with IC50 = 1.5  $\mu$ M and 2.0  $\mu$ M, resp.

L8 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN  
 1996:34891 Document No. 124:179425 Producing protein-synthetic polymer **conjugate**. Yasui, Mitsuo; Suguru, Sumita; Isamu, Uemura (Hyogo Prefectural Government, Japan). U.S. US 5473034 A 19951205, 6 pp. (English). CODEN: USXXAM. APPLICATION: US 1994-204389 19940318.

AB An aqueous solution, fine powder or suspension of a protein having free carboxyl

groups is esterified with an excess amount of polyfunctional alc. The polyfunctional alc. portion of the **conjugate** protein is further reactive with isocyanate compound or epichlorohydrin. The polyfunctional alc. portion of the **conjugate** protein may contain an unsatd. bond for graft polymerization of addition polymer onto the **conjugate** protein. Alkali-treated gelatin was esterified with allyl alc. at 50° and recovered as a powder (91% esterified carboxy), this protein could be grafted with polystyrene.

L8 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

1995:630231 Document No. 123:77786 Vinyl sulfone coupling of polyoxyalkylenes to proteins. Snow, Robert A.; Ladd, David L. (Sterling Winthrop Inc., USA). U.S. US 5414135 A 19950509, 14 pp. Cont. of U.S. Ser. No. 815, 722, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1993-153553 19931116. PRIORITY: US 1991-815722 19911230.

AB A new class of polyalkylene oxide vinyl sulfone reagents is described. Also described are a method by which these reagents can be prepared as well as a method for using them in hydrated media for the modification of proteins. The novel polymer-to-protein **conjugates** made by reacting these reagents with proteins have advantages over similar **conjugates** prepared with prior art reagents in that they are more stable against hydrolysis and retain the pos. charge carrying capacity at amine sites at which the modifying reagents are attached. Thus, methoxypolyethylene glycol was dissolved in warm THF under a N<sub>2</sub> atmospheric, cools, and treated with divinyl sulfone followed 0.1N aqueous NaOH solution

The reaction mixture was stirred at ambient temperature for 5 h, then neutralized with 0.1N HCl, and filtered. Washing with ether and extraction with chloroform gave a 79% yield of  $\alpha$ -[2-(ethenyl-sulfonyl)ethyl]- $\omega$ -methoxy-poly(oxy-1,2-ethanediyl). The **polyethylene glycol** vinyl sulfone was coupled to proteins such as bovine superoxide dismutase, interleukin-4, catalase, subtilisin, and various model peptides. Even after 6 mo, the vinyl sulfone linkage exhibited excellent stability relative to a succinate active ester linkage.

L8 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

1994:541677 Document No. 121:141677 Drug delivery systems, characterized by a photolabile linkage. Guillet, James E.; Bakhtiyari, Hamid (Medipro Sciences Ltd., Can.). PCT Int. Appl. WO 9409826 A2 19940511, 51 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1993-CA466 19931101. PRIORITY: US 1992-971996 19921030.

AB A photoactivatable drug delivery system is provided, in which a drug is combined with a photosensitive macromol. by covalent bonding, incorporation in a matrix, or encapsulation. The macromol. is large enough to prevent migration of the combination within the body, so that the combination can be implanted at a location of maximum effectiveness. The drug is released from the combination, in therapeutically active form, upon appropriate irradiation. Thus, 3-nitro-4-bromomethylbenzoic acid was treated with thionyl chloride and PEG to give a **conjugate**, which was reacted with indomethacin Cs salt to form a drug-photolabile group-polymer compound

L8 ANSWER 17 OF 19 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 1

94:419938 The Genuine Article (R) Number: NT610. PREPARATION AND PROPERTIES OF DI-(ETHYLENEGLYCOL), TRI-(ETHYLENEGLYCOL) AND POLY-(ETHYLENEGLYCOL) ESTERS OF 2-BENZOXAZOLON-3-YL-ACETIC ACID. MINCHEVA Z; STAMBOLIEVA N (Reprint); RASHKOV I. BULGARIAN ACAD SCI, INST ORGAN CHEM, BU-1113 SOFIA, BULGARIA (Reprint); BULGARIAN ACAD SCI, INST ORGAN CHEM, BU-1113 SOFIA, BULGARIA; UNIV SOFIA, DEPT CHEM, BU-1126 SOFIA, BULGARIA; UNIV SOFIA, INST POLYMERS, BU-1126 SOFIA, BULGARIA. EUROPEAN POLYMER JOURNAL (JUL 1994)



Vol. 30, No. 7, pp. 761-765. ISSN: 0014-3057. Pub. country: BULGARIA.  
Language: ENGLISH.

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB 2-Benzoxazolon-3-yl-acetic acid was esterified with diethylene glycol, triethylene glycol and polyethylene glycols with M(W) in the range of 200-1000 D by means of the dicyclohexylcarbodiimide procedure in tetrahydrofuran, resulting in the corresponding monoesters in comparatively good yields (70-92%). The products were characterized by H-1-NMR, i.r. and u.v.-spectra as well as by GPC, VPO and DSC methods. The relatively narrow molecular weight distribution was preserved in the process of the chemical modification. The degree of esterification is gradually decreasing from 91% to 44% with the increase of the length of the polyether chain. The synthesized **conjugates** are homogeneous as judged by GPC analysis, but clear evidence for heterogeneity is obtained by the more sensitive HPLC technique. The molecular mass of the **polyethylene glycols** used affects the physicochemical properties thus providing 2-benzoxazolon-3-yl-acetic acid **polyethylene glycol conjugates** of variable properties able to meet different kind of demands. We found that the **conjugate** with PEG400 is extremely useful as a substrate in the penicillin amidase catalysed transfer of 2-benzoxazolon-3-yl-acetyl moiety on 7-aminodesacetoxy-cephalosporanic acid offering a new cephem in high yield (70%).

L8 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN  
1994:586970 Document No. 121:186970 Pharmacokinetic results on naproxen prodrugs based on poly(ethylene glycol)s. Ranucci, E.; Sartore, L.; Peroni, I.; Latini, R.; Bernasconi, R.; Ferruti, P. (Dip. Ingegneria Meccanica, Univ. Brescia, Brescia, 25133, Italy). Journal of Biomaterials Science, Polymer Edition, 6(2), 141-7 (English) 1994. CODEN: JBSEEA. ISSN: 0920-5063.

AB Five prodrugs of naproxen, in which the drug was bound by ester linkages to diethylene glycol, triethylene glycol, octanediol, butyltriethylene glycol, and butyl-tetraethylene glycol, resp., were prepared and tested for their pharmacokinetic properties after oral administration. It was found that bioavailability decreased in the order, and in all cases were lower than that of the free drug.

L8 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN  
1993:490651 Document No. 119:90651 Reagents for the preparation of chromophorically labeled **polyethylene glycol**-protein **conjugates**. Ladd, David L.; Snow, Robert A. (Sterling Winthrop Pharm. Res. Div., Sterling Winthrop Inc., Malvern, PA, 19355, USA). Analytical Biochemistry, 210(2), 258-61 (English) 1993. CODEN: ANBCA2. ISSN: 0003-2697.

AB A new class of reagents for the covalent attachment of **polyethylene glycol** to proteins were prepared. These reagents are the monomethoxypolyethylene glycol esters of 4-fluoro-3-nitrobenzoic acid (I). The reaction of I with lysine  $\epsilon$ -amino groups produces a chromophore which can be used to quantitate the **polyethylene glycol** to protein molar ratio. Bovine (Zn, Cu) superoxide dismutase was used as a model protein for conjugation with I. When monomethoxypolyethylene glycol of average mol. weight 2105 was used, a **conjugate** was obtained with a **polyethylene glycol** to protein molar ratio of 8.88 retaining 100% of native enzymic activity; monomethoxypolyethylene glycol of average mol. weight 5210 yielded a **conjugate** with a **polyethylene glycol** to protein molar ratio of 9.96 retaining 73% of native enzymic activity.

=> s l1 and PEG

L9 3484 L1 AND PEG

=> s l9 and location

L10 21 L9 AND LOCATION

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PROCESSING COMPLETED FOR L10

L11 11 DUP REMOVE L10 (10 DUPLICATES REMOVED)

=> d l11 1-11 cbib abs

L11 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

2003:532863 Document No. 139:81627 Method for the oriented immobilization of proteins on MALDI target arrays. Koopman, Jens-Oliver; Blackburn, Jonathan Michael (Sense Proteomic Limited, UK). PCT Int. Appl. WO 2003056344 A2 20030710, 50 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB5882 20021220. PRIORITY: GB 2001-30747 20011221; GB 2002-16387 20020715.

AB A probe for the anal. of one or more proteins, by laser desorption/ionization mass spectrometry is disclosed. The proteins comprise a tag, which in turn comprise a biotin group. The probe comprises at least one surface comprising one or more of streptavidin, avidin or neutravidin mols. to bind the biotin group to the surface. The proteins can also carry a biotin carboxyl carrier protein, BCCP tag. The probe can form a protein array of two or more proteins at know **locations** on the surface of a chip. Methods of anal. by laser desorption/ ionization mass spectrometry using the probe are also disclosed. A scalable MALDI target volume sample volume loading kit and methods for its use are described. Thus glass and gold MALDI targets were surface coated with 1% PLL-PEG-2%-biotin solution, dried and overlaid with 0.5 mg/mL neutravidin at each position of the array, washed and dried. The prepared highly specific affinity capture surface was overlaid with biotinylated protein, incubated, washed. For MALDI anal. it was overlaid with  $\alpha$ -cyano-4-hydroxycinnamic acid in acetone.

L11 ANSWER 2 OF 11 MEDLINE on STN DUPLICATE 1

2003422902. PubMed ID: 12963999. Trastuzumab-conjugated boron-containing liposomes for tumor-cell targeting; development and cellular studies. Wei Qichun; Kullberg Erika Bohl; Gedda Lars. (Division of Biomedical Radiation Sciences, Department of Oncology, Radiology and Clinical Immunology, Rudbeck Laboratory, Uppsala University, SE-751 85 Uppsala, Sweden.. weiqichun@hotmail.com) . International journal of oncology, (2003 Oct) 23 (4) 1159-65. Journal code: 9306042. ISSN: 1019-6439. Pub. country: Greece. Language: English.

AB The goal of the present study was to investigate HER-2-targeted boron-containing liposomes as a potential drug delivery vehicle for boron neutron capture therapy (BNCT). Trastuzumab was conjugated to the distal end of PEG-DSPE-NHS in micelles and the Trastuzumab-PEG-DSPE were then transferred to preformed liposomes, either empty or loaded with water soluble boronated acridine (WSA), using the micelle transfer method. The final **conjugates** were referred to as Trastuzumab-liposome and Trastuzumab-liposome-WSA. The binding specificity, uptake, retention and internalization of Trastuzumab-liposome-WSA **conjugates** were studied in cultured SK-BR-3 cells, with regard to the targeting agent, carrier, and the load. The subcellular **location** of WSA was studied using confocal microscopy. The **conjugates** showed specific binding to the HER-2 receptors of SK-BR-3 cells. High cellular uptake and internalization of the **conjugates** was seen, reaching 132 ppm of boron in the targeted cells after 24 h. WSA was distributed mainly in the cytoplasm and was shown to have long cellular retention, with 90% and 67% of the boron

remained in the cells after 24 h and 48 h, respectively. The **conjugate** Trastuzumab-liposome-WSA could be considered as a potent drug delivery system for BNCT.

L11 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

2003:49622 Document No. 138:164365 Can nuclear localization signals enhance nuclear localization of plasmid DNA?. Nagasaki, Takeshi; Myohoji, Teruhiko; Tachibana, Taro; Futaki, Shiroh; Tamagaki, Seizo (Department of Applied and Bioapplied Chemistry, Graduate School of Engineering, Osaka City University, Osaka, 558-8585, Japan). Bioconjugate Chemistry, 14(2), 282-286 (English) 2003. CODEN: BCCHEs. ISSN: 1043-1802. Publisher: American Chemical Society.

AB Nonviral vectors are safer and more cost-effective than viral vectors but are significantly less efficient, and thus, increasing the efficiency of nonviral vectors remains an important objective. One way to overcome this problem is by stimulating the nuclear localization of exogenous genes. Nuclear localization signals (NLSs) are known to be involved in the active transport of exogenous proteins and probes into the nucleus. However, stimulation of nuclear localization of plasmid DNA has yet to be confirmed completely. In the present study, we prepared plasmid DNA-NLS peptide **conjugates** and adjusted spacer length and number introduced in an attempt to increase transfection efficiency. In comparison to **conjugates** with unmodified plasmid DNA and short spacers, we found that NLS-plasmid DNA **conjugates** with covalent bonding by diazo coupling through PEG chain (MW 3400) stimulated complexation with the nuclear transport proteins importin  $\alpha$  and importin  $\beta$ . Evaluation of transfection showed higher expression efficiency with plasmid DNA-NLS peptide **conjugates** than with unmodified plasmids. However, evaluation of intracellular trafficking after microinjection into the cytoplasm showed plasmid DNA-NLS peptide **conjugates** only within the cytoplasm; there was no NLS-plasmid stimulation of nuclear localization. Our findings suggest that stimulation of plasmid nuclear localization cannot be achieved merely by changing spacer length or chemical modifying plasmid DNA-NLS peptide **conjugates**. An addnl. mechanism must be involved.

L11 ANSWER 4 OF 11 MEDLINE on STN

DUPLICATE 2

2002680712. PubMed ID: 12440858. Selective alkylation and acylation of alpha and epsilon amino groups with PEG in a somatostatin analogue: tailored chemistry for optimized bioconjugates. Morpurgo Margherita; Monfardini Cristina; Hofland Leo J; Sergi Mauro; Orsolini Paolo; Dumont Jean M; Veronese Francesco M. (Universita degli Studi di Padova, Dipartimento Scienze Farmaceutiche, via Marzolo, 5, 35131 Padova, Italy.) Bioconjugate chemistry, (2002 Nov-Dec) 13 (6) 1238-43. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB The effects of the type and location of polymer grafting on the biological activity of different mono-PEG derivatives of the somatostatin analogue RC160 were evaluated. A chemical strategy to obtain mono-PEG alkylation or acylation of the peptide's alpha-terminal or lysil-epsilon primary amines was devised. Selective BOC protection of the two available primary amines, followed by reaction with two different PEG reagents and removal of the protecting group, was carried out. Chemical characterization, structural studies, and the evaluation of the biological activity of the bioconjugates synthesized allowed the identification of the one having characteristics more suitable for therapeutic application. This corresponds to the mono-epsilon-lysil-pegylated form, obtained by reductive alkylation, where the amine's positive charge is preserved. The results obtained suggest the importance of preliminary studies in the development of new polymer-peptide **conjugates** with improved pharmacological properties.

L11 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

2001:434839 Document No. 135:51040 Phospholipid drug carrier compositions with protected surface reactive functions. Mayer, Lawrence D.; Chiu,

Gigi; Bally, Marcel B. (Celator Technologies Inc., Can.). PCT Int. Appl. WO 2001041738 A2 20010614, 40 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-CA1494 20001211. PRIORITY: US 1999-458957 19991210.

AB The liposomes of the invention have a reactive surface that demonstrates reduced interaction with macromols. and increased blood circulation time. The reactive surface may comprise phosphatidylserine. The liposomes are protected by the presence of high levels of a hydrophilic polymer conjugated to a lipid. The invention further provides means for adjusting the appropriate ratio of hydrophilic polymer to a reactive lipid by determining the reactivity of the lipid; determining the time required for the carrier to reach its desired target **location**; determining the affinity of desired interactions with the reactive surface; and incorporating in the liposome or lipid carrier the amount of polyethylene glycol required to protect the reactive surface. Incorporation of **PEG**-DSPE at 5% in DSPC/Chol (50:45) liposomes resulted in 28 and 37% inhibition of prothrombin binding at protein-lipid ratios of 0.25:1 and 0.1:1, resp.

L11 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN  
1999:723153 Document No. 131:324165 Laundry detergent and/or fabric care compositions comprising an enzyme modified with a cellulose-binding domain. Smets, Johan; Bettiol, Jean-Luc Philippe; Boyer, Stanton Lane; Busch, Alfred (The Procter & Gamble Company, USA). PCT Int. Appl. WO 9957250 A1 19991111, 96 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US8856 19980501.

AB The present invention relates to a modified enzyme which comprises a catalytically active amino acid sequence of an enzyme, linked via a non-amino acid linking region to an amino acid sequence comprising a Cellulose Binding Domain (CBD). In one embodiment the modified enzyme comprises coupling CBD from Clostridium cellulovorans with Endolase (a cellulolytic enzyme from Hansenula insolens) with the **PEG** linker **PEG**(NPC)2. CBD **conjugates** are also prepared with Savinase (proteolytic enzyme), Purafact (amylolytic enzyme), Lipolase (lipolytic enzyme), Pulpzyme (xylanase), dextranucrase and transferases EC 2.3.2.13 and EC 2.4.1.19, Pectinex (pectinase), and laccase from Myceliophthora thermophila. The present invention further relates to laundry detergent and/or fabric care compns. comprising such modified enzyme(s). These compns. provide a higher effective concentration of the enzyme at its substrate **location** and therefore, improved enzymic benefits.

L11 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN  
1995:735501 Document No. 123:102786 Modified platelet factor 4 (PF4) compositions and therapeutic and diagnostic use. Maione, Theodore E.; Lai, Chee Kong (Repligen Corp., USA). PCT Int. Appl. WO 9512414 A1 19950511, 89 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1994-US12737 19941104. PRIORITY: US 1993-149104 19931105.

AB The invention pertains to the use of modified PF4 to inhibit angiogenesis. The modified PF4 has utility for treating angiogenic diseases and for the inhibition of endothelial cell proliferation. Also, the invention concerns modifications of PF4 which extend the half-life and facilitate

the targeting of the biol. activity of PF4 to specific **locations**. Furthermore, PF4 itself can be used to target the activities of other mols. to **locations** of angiogenesis and endothelial cell proliferation. Conjugation of recombinant PF4 (rPF4) with albumin, glycine Me ester, fluorescein derivs., **PEG**, etc. is described. Also described are construction and biol. activity of various mutant recombinant rPF4 mols. A **PEG-rPF4 conjugate** inhibited melanoma lung metastases. The **PEG-rPF4 conjugate** showed an advantageous clearance rate from the bloodstream, compared to rPF4.

L11 ANSWER 8 OF 11 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
95:207459 The Genuine Article (R) Number: QL986. FATE OF WATER-SOLUBLE POLYMERS ADMINISTERED VIA DIFFERENT ROUTES. YAMAOKA T; TABATA Y; IKADA Y (Reprint). KYOTO UNIV, BIOMED ENGN RES CTR, 53 KAWAHARA CHO, KYOTO 606, JAPAN (Reprint); KYOTO UNIV, BIOMED ENGN RES CTR, KYOTO 606, JAPAN. JOURNAL OF PHARMACEUTICAL SCIENCES (MAR 1995) Vol. 84, No. 3, pp. 349-354. ISSN: 0022-3549. Pub. country: JAPAN. Language: ENGLISH.  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB The biological fate of synthetic water-soluble polymers administered to mice by injection at different sites is described. After intraperitoneal (ip), subcutaneous (sc), and intramuscular (im) injections of (125)I-labeled poly(vinyl alcohol) (PVA) and poly(ethylene glycol) (**PEG**) with various molecular weights, the time-course of polymer concentration in the blood was measured and analyzed pharmacokinetically. The **location** of PVA in the body was similar to that of **PEG**; that is, the elimination from the injection sites and the translocation from the injection sites into the blood circulation were similar for both polymers. The elimination rate of both polymers from the injection sites increased in the order ip > sc > im. After sc and im injections of polymers, the elimination rate decreased with an increase in the molecular weight, whereas the elimination rate of polymers injected showed no molecular weight dependence over the range studied, regardless of the type of polymers used. The time-course of polymer concentration in the blood depended largely on the injection route of the polymers, and the polymer elimination from the blood circulation was enhanced with the decreasing molecular weight of polymers injected. It was concluded that the molecular weight and the injection site are the important factors that affect the concentration profile of polymers in the blood circulation.

L11 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN  
1994:541677 Document No. 121:141677 Drug delivery systems, characterized by a photolabile linkage. Guillet, James E.; Bakhtiyari, Hamid (Medipro Sciences Ltd., Can.). PCT Int. Appl. WO 9409826 A2 19940511, 51 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1993-CA466 19931101. PRIORITY: US 1992-971996 19921030.

AB A photoactivatable drug delivery system is provided, in which a drug is combined with a photosensitive macromol. by covalent bonding, incorporation in a matrix, or encapsulation. The macromol. is large enough to prevent migration of the combination within the body, so that the combination can be implanted at a **location** of maximum effectiveness. The drug is released from the combination, in therapeutically active form, upon appropriate irradiation. Thus, 3-nitro-4-bromomethylbenzoic acid was treated with thionyl chloride and **PEG** to give a **conjugate**, which was reacted with indomethacin Cs salt to form a drug-photolabile group-polymer compound

L11 ANSWER 10 OF 11 MEDLINE on STN DUPLICATE 3  
95324715. PubMed ID: 7601270. Localization of fibrinogen during aggregation of avian thrombocytes. O'Toole E T; Hantgan R R; Lewis J C. (Department of Pathology, Bowman Gray School of Medicine, Wake Forest

University, Winston-Salem, North Carolina 27157, USA. ) Experimental and molecular pathology, (1994 Dec) 61 (3) 175-90. Journal code: 0370711. ISSN: 0014-4800. Pub. country: United States. Language: English.

AB The thrombocyte is the avian equivalent of the mammalian blood platelet and is involved in hemostasis through a fibrinogen-mediated process. Although fibrinogen has been implicated as a molecular bridge between activated cells during aggregation, the **location** of this molecule and its receptor on thrombocytes has not been characterized. Pigeon fibrinogen, isolated from plasma by precipitation with **PEG**-1000 and purified over Sepharose 4B, was used to study receptor-ligand interaction. Separation of pigeon fibrinogen on SDS-PAGE resulted in three peptides of molecular mass 62, 55, and 47 kDa, which were comparable to those of human fibrinogen. The role of fibrinogen and its receptor in thrombocyte function was established by turbidimetric aggregation using thrombin as an agonist under conditions requiring  $\text{Ca}^{2+}$  and fibrinogen. Maximum response occurred using 3 mM  $\text{Ca}^{2+}$  and 100 micrograms/ml fibrinogen. Fibrinogen-dependent aggregation was inhibited by an anti-GPIIb antibody, verifying a role for fibrinogen receptors in thrombocyte function. Fibrinogen-gold **conjugates** were used to describe receptor and ligand localization on aggregated cells. Computer reconstruction was used to verify relocation of fibrinogen receptors following activation. Fibrinogen distribution changed from a dispersed state in preactivated cells to focal localization at points of cell contact and along pseudopods following activation. This selective positioning of fibrinogen suggests that a functional relocation of the receptor occurs upon thrombocyte activation, and this relocation facilitates the role of fibrinogen as a molecular bridge. These studies establish similarities between the avian and the human systems and document the conserved nature of the hemostatic process.

L11 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN  
1993:116622 Document No. 118:116622 The brain levels and blood-brain barrier protective effect of intravenous injection of polyethylene glycol-conjugated superoxide dismutase (**PEG-SOD**) in acute-hypertensively injured rat. Yoshida, Kenshi (Sch. Med., Nihon Univ., Tokyo, 173, Japan). Nihon University Journal of Medicine, 34(5), 263-72 (English) 1992. CODEN: NUMDAE. ISSN: 0546-0352.

AB The permeability of the blood-brain barrier (BBB) to polyethylene glycol-conjugated superoxide dismutase (**PEG-SOD**) and the protective effect of **PEG-SOD** on the BBB were investigated in rats subjected to norepinephrine-induced acute hypertension and appropriate control animals. An increased permeability of the BBB to  $^{125}\text{I}$ -albumin and an increase in brain water content were observed following acute hypertension. I.v. injection of **PEG-SOD** (2000 U/kg) significantly ameliorated the increased permeability and brain edema induced by acute hypertension. **PEG-SOD** was labeled with  $^{125}\text{I}$  and injected i.v. at 30 min before acute hypertension in exptl. rats (acute hypertension group) or control rats (normotensive group). The normotensive group revealed low levels of brain and cerebrospinal fluid (CSF) **PEG-SOD** at 90 min after the injection of **PEG-SOD** yielding values of 0.029 U/g wet weight and 0.052 U/mL, resp. Significant 2.5- and 7-fold increases in the brain and CSF levels of **PEG-SOD**, resp., were observed in the acute hypertension group, as compared to those of the normotensive group. These results imply that oxygen free radicals play a significant role in the BBB permeability and brain water content. However, questions regarding the scavenging site of **PEG-SOD** remain unclarified due to its poor accessibility to the BBB and the indistinct cellular **location** of the increased brain **PEG-SOD**.

=> s l1 and B cell anergy

4 FILES SEARCHED...

L12 5 L1 AND B CELL ANERGY

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 PROCESSING COMPLETED FOR L12  
 L13 5 DUP REMOVE L12 (0 DUPLICATES REMOVED)

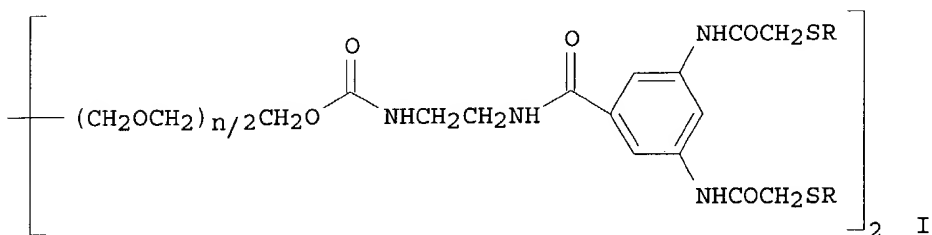
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L13 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
 2000:307077 Document No. 132:320935 Induction of humoral anergy using  
 immunogen **conjugates** lacking T-cell epitopes. Coutts, Stephen  
 M.; Barstad, Paul A.; Iverson, G. Michael; Jones, David S. (La Jolla  
 Pharmaceutical Company, USA). U.S. US 6060056 A 20000509, 30 pp.,  
 Cont.-in-part of U.S. 5,268,454. (English). CODEN: USXXAM. APPLICATION:  
 US 1993-118055 19930908. PRIORITY: US 1991-652648 19910208.

AB The authors disclose the preparation of **conjugates** of non-immunogenic  
 carrier mols. with B-cell epitopes that possess ability to suppress  
 antigen-specific antibody responses. In one example, mice were primed  
 with the main immunogenic region of the acetylcholine receptor.  
 Subsequent immunization of these mice with a B-cell epitope peptide,  
 lacking the ability to activate primed T-cells, led to a specific  
 suppression of the anti-receptor antibody response. In a second example,  
 mice were primed with the bee venom allergen, mellitin. Immunization with  
 peptides conjugated to lysine-glutamate copolymer suppressed the  
 anti-mellitin response.

L13 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN  
 1995:892826 Document No. 124:290272 Preparation of chemically-defined  
 non-polymeric valency platform molecules and **conjugates**  
 thereof.. Coutts, Stephen; Jones, David S.; Livingston, Douglas Alan; Yu,  
 Lin (La Jolla Pharmaceutical Co., Can.). Eur. Pat. Appl. EP 642798 A2  
 19950315, 76 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB,  
 GR, IE, IT, LI, LU, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION:  
 EP 1993-309720 19931203. PRIORITY: US 1993-118055 19930908; US  
 1993-142598 19931022; US 1993-152506 19931115; EP 1993-309288 19931122.

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AB **Conjugates** comprising biol. or chemical mols., including  
 polynucleotide duplexes of at least 20 base pairs that have significant  
 binding activity for human lupus anti-dsDNA autoantibodies, reacted with  
 valency platforms G1(T1)n, G2[L2J2Z2(pT2)]m [G1, G2 = null, (branched)  
 chain containing 1-2000 atoms selected from C, N, O, Si, P, S; T1, T2 = NHR,  
 CONHNHR, NHNHR, CO2H, CO2R1, COX, SO2X, SH, OH, etc.; R = H, alkyl,  
 cycloalkyl, aralkyl; R1 = N-succinimidyl, p-nitrophenyl,  
 pentafluorophenyl, etc.; X = halo, other leaving group; L2 = null, O, NR,  
 S; J2 = null, CO, CS; Z2 = radical containing 1-200 atoms selected from C, H,  
 N, O, Si, P, S, and containing attachment sites for functional groups; n, m =  
 1-32; p = 1-8; with provisos], were prepared Thus, title **conjugate**  
 (I; R = H-Trp-Ile-Lys-Arg-Lys-Arg-Gln-Gln-Lys-Cys-Gly-OH, bound through a  
 cysteine S atom; n = approx. 74) (preparation given) at 1000 µg/mouse in  
 mice primed and boosted with the parent protein melittin gave an 86.8%  
 reduction in peptide specific plaque forming cells.

L13 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

1994:29249 Document No. 120:29249 Two separate mechanisms of T-cell clonal anergy to Mls-1a. Yui, Katsuyuki; Ishida, Yasuo; Katsumata, Makoto; Komori, Shinji; Chused, Thomas M.; Abe, Ryo (Dep. Pathol., Univ. Pennsylvania, Philadelphia, PA, 19104-6082, USA). Journal of Immunology, 151(11), 6062-75 (English) 1993. CODEN: JOIMA3. ISSN: 0022-1767.

AB T cell tolerance to superantigen can be mediated by clonal anergy in which Ag-specific mature T cells are phys. present but are not able to mount an immune response. The authors induced T cell unresponsiveness to minor lymphocyte stimulations locus antigen (Mls)-1a in mice transgenic for TCR V $\beta$ 8.1 in three different systems: injection of Mls-1a spleen cells; mating with Mls-1a mice; and bone marrow (BM) chimeras in which Mls-1a is present only on nonhematopoietic cells. CD4+8-V $\beta$ 8.1+ cells from all these groups did not proliferate in response to irradiated spleen cells from Mls-1a mice. The authors compared the response of these cells by T cell/stimulator cell **conjugate** formation, Ca<sup>2+</sup> mobilization, and proliferation assays. The mechanisms underlying the unresponsiveness of these T cells appear to differ. CD4+8-V $\beta$ 8.1+ cells from Mls-1a spleen cell-injected mice mobilized cytoplasmic Ca<sup>2+</sup> but proliferated at a reduced level in response to crosslinking with anti-TCR mAb. However, these cells formed **conjugates**, mobilized Ca<sup>2+</sup>, and proliferated in response to Mls-1a when activated B cells were used as stimulators, although they produced reduced levels of IL-2. In Mls-1a/b V $\beta$ 8.1 transgenic mice, a subset in CD4+8-V $\beta$ 8.1+ cells did not mobilize cytoplasmic Ca<sup>2+</sup> after TCR crosslinking. Their **conjugate** formation, Ca<sup>2+</sup> mobilization, or proliferation in response to Mls-1a on activated B cells was undetectable. Finally, CD4+8-V $\beta$ 8.1+ cells from the BM chimeras proliferated to TCR crosslinking at a partially reduced level and formed **conjugates**, mobilized Ca<sup>2+</sup>, and proliferated in response to Mls-1a on activated B cells. These features suggest that the mechanisms underlying the maintenance of anergy in Mls-1a spleen cell-injected mice are distinct from those in Mls-1a mice.

L13 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

1992:620072 Document No. 117:220072 Composition for inducing humoral anergy to an immunogen. Barstad, Paul Arlyn; Iverson, Gilbert Michael (La Jolla Pharmaceutical Co., USA). Eur. Pat. Appl. EP 498658 A2 19920812, 14 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1992-301036 19920207. PRIORITY: US 1991-652648 19910208.

AB A composition for inducing specific **B cell anergy** to an immunogen comprises a **conjugate** of a nonimmunogenic polymer, i.e. a copolymer of D-lysine and D-glutamic acid, and an analog of the immunogen that (a) binds specifically to B cells to which the immunogen binds specifically and (b) lacks a T cell epitope. **Conjugates** are useful for treatment of antibody-mediated pathol. caused by foreign or self immunogens. Two peptides (L-42 and L-53), corresponding to residues 61-77 and 112-127 of  $\alpha$ -subunits of the acetylcholine receptors of Torpedo californicus, resp., were reduced, desalted and reacted with D-glutamic acid-D-lysine copolymer. The L-53 **conjugate** suppressed antibody formation to L-53 but not to L-42. The L-42 **conjugate** did not suppress the antibody response to either L-42 or L-53 but rather may have increased antibody production to L-42.

L13 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

1989:182122 Document No.: PREV198987093388; BA87:93388. POSTNATAL B CELL DEVELOPMENT INFLUENCE OF TRINITROBENZENESULFONIC ACID TREATMENT DURING PREGNANCY. ZOLLER M [Reprint author]. INST RADIOL PATHOPHYSIOL, GERMAN CANCER RES CENT, IM NEUENHEIMER FELD 280, D-6900 HEIDELBERG, FRG. European Journal of Immunology, (1988) Vol. 18, No. 12, pp. 1931-1936. CODEN: EJIMAF. ISSN: 0014-2980. Language: ENGLISH.

AB Prenatal treatment with a reactive hapten may be well suited for analyzing the establishment of self tolerance because the hapten binds ubiquitously to proteins and cells and persists for a long period in the developing



organism. Based on this consideration, pregnant BALB/c mice were treated with 2,4,6-trinitrobenzenesulfonic acid (TNBS), searching for differences in 2,4,6-trinitrophenyl CTNP) responsiveness in their offspring as compared to litters of untreated mice. The frequency of TNP-specific T-independent B cells of litters from TNBS-treated mothers was very low at birth and remained below 10% of controls until the age of 42 days. On the contrary, in 8-day-old prenatally TNBS-treated litters, the frequency of TNP-specific T-dependent B cells was higher than in controls. Expansion of TNP-specific B cells after antigenic stimulation of control mice started at the age of 3-4 weeks and expansion rates increased with age, while in prenatally TNBS-treated mice, significant expansion rates were seen at the age of 2 weeks only. Yet, after restimulation with TNP-lipopolysaccharide or with a TNP-anti-TNP conjugate, but not after restimulation with TNP-ovalbumin, similar numbers of plaque-forming cells (PFC) were observed with spleen cells of prenatally untreated and TNBS-treated mice, the latter revealing an exceptional predominance of IgG PFC. Thus, TNP-specific B cells were not deleted, but prenatal TNBS treatment resulted in an altered composition of TNP-specific B cell subpopulations, their regulation differing qualitatively from the one observed in prenatally untreated mice.

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=> s (Coutts s?/au or Jones d?/au or livingston d?/au or Yu l?/au)
L14      51519 (COUTTS S?/AU OR JONES D?/AU OR LIVINGSTON D?/AU OR YU L?/AU)
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=> s l14 and valency platform
L15      15 L14 AND VALENCY PLATFORM
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=> dup remove l15
PROCESSING COMPLETED FOR L15
L16      14 DUP REMOVE L15 (1 DUPLICATE REMOVED)
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=> d l16 1-14 chib abs
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L16 ANSWER 1 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2002:609797 Document No.: PREV200200609797. Valency platform
molecules comprising carbamate linkages. Jones, David S.
[Inventor, Reprint author]. San Diego, CA, USA. ASSIGNEE: La Jolla
Pharmaceutical Company. Patent Info.: US 6458953 October 01, 2002.
Official Gazette of the United States Patent and Trademark Office Patents,
(Oct. 1, 2002) Vol. 1263, No. 1. http://www.uspto.gov/web/menu/patdata.htm
1. e-file.
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AB This invention pertains generally to valency molecules, such as
valency platform molecules which act as scaffolds to
which one or more molecules may be covalently tethered to form a
conjugate. More particularly, the present invention pertains to
valency platform molecules which comprise a carbamate
linkage (i.e., --O--C(dbdO)--Nlt;). In one aspect, the present invention
pertains to valency platforms comprising carbamate
linkages, which molecules have the structure of any one of Formulae I, II,
or III, shown in FIG. 1. In one aspect, the present invention pertains to
valency platforms comprising carbamate linkages, which
molecules have the structure of any one of Formulae IV, V, or VI, shown in
FIG. 8. The present invention also pertains to methods of preparing such
valency platform molecules, conjugates comprising such
valency platform molecules, and methods of preparing
such conjugates.
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L16 ANSWER 2 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2002:423913 Document No.: PREV200200423913. APL immunoreactive peptides,
conjugates thereof and methods of treatment for APL antibody-mediated
pathologies. Victoria, Edward Jess [Inventor, Reprint author]; Marquis,
David Matthew [Inventor]; Jones, David S. [Inventor]; Yu,
Lin [Inventor]. San Diego, CA, USA. ASSIGNEE: La Jolla Pharmaceutical
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Company. Patent Info.: US 6410775 June 25, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (June 25, 2002) Vol. 1259, No. 4. <http://www.uspto.gov/web/menu/patdata.html>. e-file. CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB aPL analogs that (a) bind specifically to B cells to which an aPL epitope binds and are disclosed. Optimized analogs lack T cell epitope(s) are useful as conjugates for treating aPL antibody-mediated diseases. Conjugates comprising aPL analogs and nonimmunogenic **valency platform** molecules are provided as are novel nonimmunogenic **valency platform** molecules and linkers. Methods of preparing and identifying said analogs, methods of treatment using said analogs, methods and compositions for preparing conjugates of said analogs and diagnostic immunoassays for aPL antibodies are disclosed.

L16 ANSWER 3 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN 2002:378035 Document No.: PREV200200378035. Conjugates comprising galactose alpha1,3 galactosyl epitopes and methods of using same. Jack, Richard M. [Inventor, Reprint author]; Jones, David S. [Inventor]; Yu, Lin [Inventor]. Del Mar, CA, USA. ASSIGNEE: La Jolla Pharmaceutical Company. Patent Info.: US 6399578 June 04, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (June 4, 2002) Vol. 1259, No. 1. <http://www.uspto.gov/web/menu/patdata.html>. e-file. CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB This invention provides conjugates useful for xenotransplantation which comprise a galactose alpha1,3 galactosyl (alphaGal) epitope conjugated to a **valency platform** molecule, preferably a chemically defined **valency platform** molecule which allows precise valency. The invention also provides compositions comprising these conjugates, and methods (such as methods for inducing tolerance) using these conjugates and compositions.

L16 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN 2001:903935 Document No. 136:54229 Multivalent platform molecules comprising high molecular weight polyethylene oxide. Jones, David S. (La Jolla Pharmaceutical Company, USA). PCT Int. Appl. WO 2001093914 A2 20011213, 78 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US18446 20010607. PRIORITY: US 2000-PV210439 20000608.

AB **Valency platform** mols. comprising high mol. weight polyethylene oxide groups are provided, as well as conjugates with biol. active mols., and methods for their preparation The high mol. weight polyethylene oxide group has mol. weight at least 40,000 Daltons. In one embodiment, a composition comprising the **valency platform** mols. is provided, wherein the mols. have a polydispersity less than about 1.2. Conjugates of the **valency platform** mol. and a biol. active mol., such as a saccharide, poly(saccharide), amino acid, poly(amino acid), nucleic acid or lipid also are provided. Also provided are pharmaceutically acceptable compns. comprising the conjugates disclosed herein and a pharmaceutically acceptable carrier, as well as methods of making and using the conjugates and compns.

L16 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN 2000:881116 Document No. 134:56426 Preparation of molecules containing aminoxy groups as **valency platform** molecules for preparation of bioconjugates.. Jones, David S.; Ton-nu, Huong-thu; Xie, Fang; Tao, Anping; Xu, Tong; Hammaker, Jeffrey Robert (La Jolla Pharmaceutical Co., USA). PCT Int. Appl. WO 2000075105 A1 20001214,

113 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US15968 20000608. PRIORITY: US 1999-PV138260 19990608.

AB Oxyalkylene mols. containing  $\geq 3$  aminoxy groups were prepared Thus,  $\text{MeO}(\text{CH}_2\text{CH}_2\text{O})_n\text{CH}_2\text{CH}_2\text{O}_2\text{CN}[\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{O}_2\text{CN}(\text{CH}_2)_5\text{NHCO}(\text{CH}_2)_5\text{NH}_2]_2$  ( $n = \text{approx. } 503$ ) (preparation outlined) was stirred with Domain 1 polypeptide  $\beta 2\text{GPI}$ -glyoxylic acid reaction product to give the tetraadduct, which at  $0.17 \text{ nmol/rat}$  gave  $61\%$  suppression of anti-Domain 1 antibody in immunized rats.

L16 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
2000:401844 Document No. 133:42177 Conjugates comprising galactose alpha 1,3 galactosyl epitopes and methods of using same. Jack, Richard M.; Jones, David; Yu, Lin (La Jolla Pharmaceutical Company, USA). PCT Int. Appl. WO 2000034296 A2 20000615, 100 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US29338 19991209. PRIORITY: US 1998-PV111644 19981209; US 1999-PV160997 19991023; US 1999-457913 19991208.

AB This invention provides conjugates useful for xenotransplantation which comprise a galactose  $\alpha 1,3$  galactosyl ( $\alpha\text{Gal}$ ) epitope conjugated to a **valency platform** mol., preferably a chemical defined **valency platform** mol. which allows precise valency. The invention also provides compns. comprising these conjugates, and methods (such as methods for inducing tolerance) using these conjugates and compns.

L16 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
2000:401781 Document No. 133:44002 Dendritic molecular scaffolds acting as templates comprising carbamate linkages. Jones, David S. (La Jolla Pharmaceutical Company, USA). PCT Int. Appl. WO 2000034231 A1 20000615, 127 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US29339 19991209. PRIORITY: US 1998-PV111641 19981209; US 1999-457607 19991208.

AB This invention pertains generally to valency mols., such as **valency platform** mols. which act as scaffolds to which one or more mols. may be covalently tethered to form a conjugate. More particularly, the present invention pertains to **valency platform** mols. which comprise a carbamate linkage (i.e.,  $-\text{O}-\text{C}(=\text{O})-\text{N}<$ ). The present invention also pertains to methods of preparing such **valency platform** mols., conjugates comprising such **valency platform** mols., and methods of preparing such conjugates.

L16 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
2000:401689 Document No. 133:38230 Methods and formulations based on epitope-presenting carriers for reducing circulating antibodies. Jack,

Richard M.; Jones, David S.; Yu, Lin; Engle, Steven B.  
(La Jolla Pharmaceutical Company, USA). PCT Int. Appl. WO 2000033887 A2  
20000615, 74 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB,  
BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE,  
GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,  
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,  
SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM,  
CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT,  
SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US29336  
19991209. PRIORITY: US 1998-PV111639 19981209; US 1999-457875 19991208.

AB The invention provides methods for reducing circulating levels of  
antibodies, particularly disease-associated antibodies. The methods entail  
administering effective amts. of epitope-presenting carriers to an  
individual. In other embodiments, ex vivo methods for reducing  
circulating levels of antibodies are provided which employ  
epitope-presenting carriers. For example, an octameric toleragen LJP 920  
was prepared and used for treating two rhesus monkeys i.v. at a dose of 20  
mg/kg daily for 7 days. At day 8, IgG anti- $\alpha$ Gal levels were  
decreased by 11%, while control animals showed little change. Similarly,  
there was a diminution of 18% in IgM anti- $\alpha$ Gal levels in one monkey  
and 5% in the replicate animal. By contrast, IgM anti- $\alpha$ Gal levels  
in the control animals did not change in one animal and increased in the  
replicate animal. The octamer was more efficient than the tetramer LJP  
712 at clearing IgM anti- $\alpha$ Gal, indicating that increased valency  
results in a more efficacious mol.

L16 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
1999:795964 Document No. 132:49017 Therapeutic and diagnostic domain 1 of  
human  $\beta$ 2GPI polypeptides and methods of using same. Marquis, David  
M.; Iverson, Gilbert M.; Victoria, Edward J.; Jones, David S.;  
Linnik, Matthew D. (La Jolla Pharmaceutical Company, USA). PCT Int. Appl.  
WO 9964595 A1 19991216, 159 pp. DESIGNATED STATES: W: AE, AL, AM, AT,  
AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB,  
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,  
SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,  
BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY,  
DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE,  
SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US13194  
19990609. PRIORITY: US 1998-88656 19980609; US 1998-103088 19981005; US  
1999-328199 19990608.

AB Provided are domain 1 of  $\beta$ 2GPI polypeptides, polynucleotides encoding  
them, mimetics of these polypeptides, and methods using domain 1 of  
 $\beta$ 2GPI polypeptides and mimetics. Domain 1 of  $\beta$ 2GPI has been  
shown to bind to anti-cardiolipin ( $\beta$ 2GPI-dependent anti-phospholipid)  
antibodies, which are associated with several pathologies, such as thrombosis  
and fetal loss. The domain 1 of  $\beta$ 2GPI polypeptides may be used to  
detect  $\beta$ 2GPI-dependent anti-phospholipid antibodies in a sample.  
Further provided are methods of inducing tolerance using these domain 1 of  
 $\beta$ 2GPI polypeptides. Synthesis of **valency platform**  
comps. and conjugation of the comps. with domain 1 were also  
demonstrated.

L16 ANSWER 10 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
2002:62199 Document No.: PREV200200062199. Chemically-defined non-polymeric  
**valency platform** molecules and conjugates thereof.  
Coutts, S. M. [Inventor]; Jones, D. S. [Inventor];  
Livingston, D. A. [Inventor]; Yu, L. [Inventor]. Rancho  
Santa Fe, Calif., USA. ASSIGNEE: LA JOLLA PHARMACEUTICAL COMPANY. Patent  
Info.: US 5606047 Feb. 25, 1997. Official Gazette of the United States  
Patent and Trademark Office Patents, (Feb. 25, 1997) Vol. 1195, No. 4, pp.  
2594-2595. print.  
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

L16 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

1998:1383 Document No. 128:61804 aPL immunoreactive peptides and their conjugates for treatment of aPL antibody-mediated pathologies. Victoria, Edward Jess; Marquis, David Matthew; Jones, David S.; Yu, Lin (Lajolla Pharmaceutical Company, USA; Victoria, Edward Jess; Marquis, David Matthew; Jones, David S.; Yu, Lin). PCT Int. Appl. WO 9746251 A1 19971211, 155 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US10075 19970606. PRIORITY: US 1996-660092 19960606; US 1996-760508 19961205.

AB APL analogs that bind specifically to B cells to which an aPL epitope binds are disclosed. Optimized analogs lacking T cell epitope(s) are useful as conjugates for treating aPL antibody-mediated diseases. Conjugates comprising aPL analogs and nonimmunogenic **valency platform** mols. are provided as are novel nonimmunogenic **valency platform** mols. and linkers. Methods of preparing and identifying said analogs, methods of treatment using said analogs, methods and compns. for preparing conjugates of said analogs and diagnostic immunoassays for aPL antibodies are disclosed.

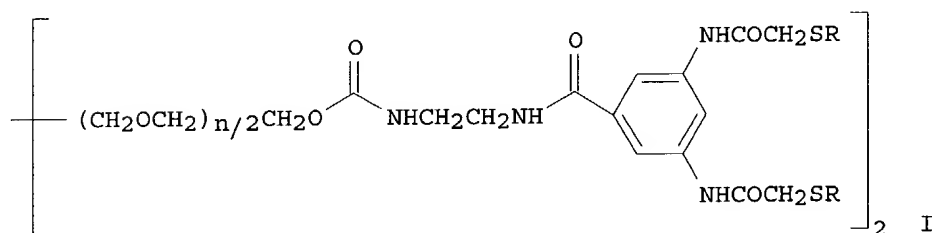
L16 ANSWER 12 OF 14 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 1

2002:48444 Document No.: PREV200200048444. Chemically-defined non-polymeric **valency platform** molecules and conjugates thereof. Coutts, S. M. [Inventor]; Jones, D. S. [Inventor]; Livingston, D. A. [Inventor]; Yu, L. [Inventor]. Rancho Santa Fe, Calif., USA. ASSIGNEE: LA JOLLA PHARMACEUTICAL COMPANY. Patent Info.: US 5552391 Sept. 3, 1996. Official Gazette of the United States Patent and Trademark Office Patents, (Sept. 3, 1996) Vol. 1190, No. 1, pp. 437-438. print. CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

L16 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

1995:892826 Document No. 124:290272 Preparation of chemically-defined non-polymeric **valency platform** molecules and conjugates thereof.. Coutts, Stephen; Jones, David S.; Livingston, Douglas Alan; Yu, Lin (La Jolla Pharmaceutical Co., Can.). Eur. Pat. Appl. EP 642798 A2 19950315, 76 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1993-309720 19931203. PRIORITY: US 1993-118055 19930908; US 1993-142598 19931022; US 1993-152506 19931115; EP 1993-309288 19931122.

GI



AB Conjugates comprising biol. or chemical mols., including polynucleotide

duplexes of at least 20 base pairs that have significant binding activity for human lupus anti-dsDNA autoantibodies, reacted with **valency platforms** G1(T1)n, G2[L2J2Z2(pT2)]m [G1, G2 = null, (branched) chain containing 1-2000 atoms selected from C, N, O, Si, P, S; T1, T2 = NHR, CONHNHR, NHNHR, CO2H, CO2R1, COX, SO2X, SH, OH, etc.; R = H, alkyl, cycloalkyl, aralkyl; R1 = N-succinimidyl, p-nitrophenyl, pentafluorophenyl, etc.; X = halo, other leaving group; L2 = null, O, NR, S; J2 = null, CO, CS; Z2 = radical containing 1-200 atoms selected from C, H, N, O, Si, P, S, and containing attachment sites for functional groups; n, m = 1-32; p = 1-8; with provisos], were prepared Thus, title conjugate (I; R = H-Trp-Ile-Lys-Arg-Lys-Arg-Gln-Gln-Lys-Cys-Gly-OH, bound through a cysteine S atom; n = approx. 74) (preparation given) at 1000 µg/mouse in mice primed and boosted with the parent protein melittin gave an 86.8% reduction in peptide specific plaque forming cells.

L16 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN  
 1994:261341 Document No. 120:261341 Conjugates of biologically stable polyfunctional molecules and polynucleotides for treating systemic lupus erythematosus (SLE). Conrad, Michael J.; **Coutts, Stephen** (La Jolla Pharmaceutical Co., USA). U.S. US 5276013 A 19940104, 21 pp. Cont.-in-part of U.S. 5,162,515. (English). CODEN: USXXAM. APPLICATION: US 1992-914869 19920715. PRIORITY: US 1990-466138 19900116; US 1990-494118 19900313.

AB Chemical defined conjugates are disclosed which consist of biol. stable **valency platform** mols., e.g. copolymers of D-glutamic acid and D-lysine or PEG, and polynucleotide duplexes of ≥20 base pairs that have significant binding activity for human lupus anti-dsDNA autoantibodies. The duplexes are preferably homogeneous in length structure and are bound to the **valency platform** mol. via reaction between a functional group located at or proximate a terminus of each duplex and functional groups on the **valency platform** mol. The conjugates are tolerogens for human SLE. Thus a conjugate of D-glutamic acid-D-lysine copolymer with (AC)30:(TG)30 was prepared and tested as a tolerogen in a murine model for human SLE.

=> s l14 and conjugate  
 L17 326 L14 AND CONJUGATE

=> s l17 and peptide analog  
 L18 1 L17 AND PEPTIDE ANALOG

=> d l18 cbib abs

L18 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN  
 2001:224355 Document No. 134:265135 B-cell tolerogens for treatment for pathologies mediated by antibodies to phospholipids. Victoria, Edward Jess; Marquis, David Matthew; **Jones, David S.; Yu, Lin** (La Jolla Pharmaceutical Company, USA). U.S. US 6207160 B1 20010327, 113 pp., Cont.-in-part of U.S. 5,874,409. (English). CODEN: USXXAM. APPLICATION: US 1996-660092 19960606. PRIORITY: US 1995-482651 19950607.

AB The authors disclose analogs of anti-phospholipid antibody (aPL) epitopes that (a) bind specifically to B cells to and (b) do not induce T-cell activation. In addition, the authors disclose the preparation of non-immunogenic tetravalent scaffolds to which the synthetic tolerogens can be attached.

=> dup remove l17  
 PROCESSING COMPLETED FOR L17  
 L19 161 DUP REMOVE L17 (165 DUPLICATES REMOVED)

=> s l19 and branching  
 L20 0 L19 AND BRANCHING

=> d 119 1-161 cbib abs

L19 ANSWER 1 OF 161 MEDLINE on STN DUPLICATE 1  
2004105262. PubMed ID: 14997198. Detection of curcumin and its metabolites in hepatic tissue and portal blood of patients following oral administration. Garcea G; **Jones D J L**; Singh R; Dennison A R; Farmer P B; Sharma R A; Steward W P; Gescher A J; Berry D P. (Cancer Biomarkers and Prevention Group, Department of Cancer Studies and Biochemistry, University of Leicester, 5th Floor Robert Kilpatrick Clinical Sciences Building, Leicester LE2 7LX, UK.. gg43@le.ac.uk) . British journal of cancer, (2004 Mar 8) 90 (5) 1011-5. Journal code: 0370635. ISSN: 0007-0920. Pub. country: England: United Kingdom. Language: English.

AB Studies in vitro and in animal models of colorectal and hepatocellular cancers suggest that curcumin is an effective chemopreventive agent. In this pilot trial, we investigated whether oral administration of curcumin results in concentrations of the agent in normal and malignant human liver tissue, which are sufficient to elicit pharmacological activity. In total, 12 patients with hepatic metastases from colorectal cancer received 450-3600 mg of curcumin daily, for 1 week prior to surgery. Levels of curcumin and its metabolites were measured by HPLC in portal and peripheral blood, bile and liver tissue. Curcumin was poorly available, following oral administration, with low nanomolar levels of the parent compound and its glucuronide and sulphate **conjugates** found in the peripheral or portal circulation. While curcumin was not found in liver tissue, trace levels of products of its metabolic reduction were detected. In patients who had received curcumin, levels of malondialdehyde-DNA (M(1)G) adduct, which reflect oxidative DNA changes, were not decreased in post-treatment normal and malignant liver tissue when compared to pretreatment samples. The results suggest that doses of curcumin required to furnish hepatic levels sufficient to exert pharmacological activity are probably not feasible in humans.

L19 ANSWER 2 OF 161 MEDLINE on STN DUPLICATE 2  
2004058459. PubMed ID: 14760392. Pharmacokinetics in mice and growth-inhibitory properties of the putative cancer chemopreventive agent resveratrol and the synthetic analogue trans 3,4,5,4'-tetramethoxystilbene. Sale S; Verschoyle R D; Boocock D; **Jones D J L**; Wilsher N; Ruparelia K C; Potter G A; Farmer P B; Steward W P; Gescher A J. (Department of Oncology, University of Leicester, Leicester, UK. ) British journal of cancer, (2004 Feb 9) 90 (3) 736-44. Journal code: 0370635. ISSN: 0007-0920. Pub. country: England: United Kingdom. Language: English.

AB Resveratrol (trans-3,5,4'-trihydroxystilbene) is a naturally occurring polyphenol with cancer chemopreventive properties in preclinical models of carcinogenesis, including those of colorectal cancer. Recently, a variety of analogues of resveratrol have been synthesised and investigated in in vitro assays. One analogue, 3,4,5,4'-tetramethoxystilbene (DMU 212), showed preferential growth-inhibitory and proapoptotic properties in transformed cells, when compared with their untransformed counterparts. As part of a chemoprevention drug development programme, the pharmacokinetic properties of DMU 212 were compared with those of resveratrol in the plasma, liver, kidney, lung, heart, brain and small intestinal and colonic mucosa of mice. DMU 212 or resveratrol (240 mg kg(-1)) were administered intragastrically, and drug concentrations were measured by HPLC. Metabolites were characterised by cochromatography with authentic reference compounds and were identified by mass spectrometry. The ratios of area of plasma or tissue concentration vs time curves of resveratrol over DMU 212 (AUC(res)/AUC(DMU212)) for the plasma, liver, small intestinal and colonic mucosa were 3.5, 5, 0.1 and 0.15, respectively. Thus, resveratrol afforded significantly higher levels than DMU 212 in the plasma and liver, while DMU 212 exhibited superior availability compared to resveratrol in the small intestine and colon. Resveratrol was metabolised to its sulphate or glucuronate **conjugates**, while DMU 212 underwent metabolic hydroxylation or

single and double O-demethylation. DMU 212 and resveratrol inhibited the growth of human-derived colon cancer cells HCA-7 and HT-29 in vitro with IC(50) values of between 6 and 26 microM. In the light of the superior levels achieved in the gastrointestinal tract after the administration of DMU 212, when compared to resveratrol, the results provide a good rationale to evaluate DMU 212 as a colorectal cancer chemopreventive agent.

L19 ANSWER 3 OF 161 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 3

2004174688 EMBASE The Role of Metabolism in 3,4-(±)-Methylenedioxymphetamine and 3,4-(±)-Methylenedioxymphetamine (Ecstasy) toxicity. Monks T.J.; Jones D.C.; Bai F.; Lau S.S.. T.J. Monks, Dept. of Pharmacology and Toxicology, College of Pharmacy, University of Arizona, 1703, East Mabel Street, Tucson, AZ 85721-0207, United States. scouser@pharmacy.arizona.edu. Therapeutic Drug Monitoring 26/2 (132-136) 2004.  
Refs: 56.

ISSN: 0163-4356. CODEN: TDMODV. Pub. Country: United States. Language: English. Summary Language: English.

AB 3,4-Methylenedioxymphetamine (MDA) and 3,4-methylenedioxymphetamine (MDMA, ecstasy) are ring-substituted amphetamine derivatives with stimulant and hallucinogenic properties. The recreational use of these amphetamines, especially MDMA, is prevalent despite warnings of irreversible damage to the central nervous system. MDA and MDMA are primarily serotonergic neurotoxicants. Because (1) neither MDA nor MDMA produces neurotoxicity when injected directly into brain, (2) intracerebroventricular (ICV) administration of some major metabolites of MDA and MDMA fails to reproduce their neurotoxicity, (3)  $\alpha$ -methyldopamine ( $\alpha$ -MeDA) and N-methyl- $\alpha$ -MeDA are metabolites of both MDA and MDMA, (4)  $\alpha$ -MeDA and N-methyl- $\alpha$ -MeDA are readily oxidized to the corresponding ortho-quinones, which can undergo conjugation with glutathione (GSH), and (5) quinone thioethers exhibit a variety of toxicologic activities, we initiated studies on the potential role of thioether metabolites of  $\alpha$ -MeDA and N-methyl- $\alpha$ -MeDA in the neurotoxicity of MDA and MDMA. Our studies have revealed that the thioether **conjugates** stimulate the acute release of serotonin, dopamine, and norepinephrine and produce a behavioral response commensurate with the "serotonin syndrome." Direct injection of the **conjugates** into rat brain also produces long-term depletions in serotonin (5-HT) concentrations, elevations in GFAP expression, and activation of microglial cells. The data are consistent with the view that thioether metabolites of  $\alpha$ -MeDA and N-methyl- $\alpha$  MeDA contribute to the neurotoxicity of the parent amphetamines.

L19 ANSWER 4 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

2003:836764 Document No. 139:333095 Colon tumor-specific binding peptides, and therapeutic ad diagnostic uses thereof. Kelly, Kimberly A.; Jones, David A. (University of Utah Research Foundation, USA).

PCT Int. Appl. WO 2003086284 A2 20031023, 42 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US10630 20030407. PRIORITY: US 2002-PV369850 20020405.

AB Phage display was used to screen peptide libraries that distinguish between well-differentiated (HCT116) and poorly-differentiated colon carcinoma cells (HT29). The screening protocol used selection and subtraction on intact, viable cells, resulting in phage libraries exhibiting high binding selectivity for the poorly-differentiated HT29



cells. A nine amino acid, disulfide-constrained peptide (RPM) was identified that selectively bound and was internalized into colon cancer cells. The peptide may be used to detect colon cancer cells and also may be used to selectively deliver therapeutic agents to the cells.

L19 ANSWER 5 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

2003:912560 Document No. 139:386377 Controllably degradable polymeric biomolecule or drug carrier and method of synthesizing said carrier. Yu, Lei; Du, Fusheng; Ji, Shouping; Matsumoto, Kenji (USA). U.S. Pat. Appl. Publ. US 2003215395 A1 20031120, 31 pp. (English). CODEN: USXXCO. APPLICATION: US 2002-270788 20021011. PRIORITY: US 2002-PV378164 20020514.

AB The present invention provides a controllably degradable cationic polymer for delivery of biomols. (nucleic acids, peptides, etc.), drugs, mols. used in medical imaging applications, sensitizing agents used in cancer treatments, and mols. used in tissue engineering. The present invention also provides a method for synthesizing the polymer according to the present invention. A cationic polymer was prepared from polyethylenimine oligomer and 1,3-butanediol diacrylate for a gene delivery system.

L19 ANSWER 6 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 4

2003:1064429 The Genuine Article (R) Number: 748XL. (S)-2-(Methoxydiphenylmethyl)-1-(thiophen-3-ylmethyl)pyrrolidine. Martin E; Winfrey A L; Human J B; Carlin C Z; Jones D S (Reprint); Ogle C A. Univ N Carolina, Dept Chem, 9201 Univ City Blvd, Charlotte, NC 28223 USA (Reprint); Univ N Carolina, Dept Chem, Charlotte, NC 28223 USA. ACTA CRYSTALLOGRAPHICA SECTION E-STRUCTURE REPORTS ONLINE (DEC 2003) Vol. 59, Part 12, pp. O1970-O1971. Publisher: BLACKWELL MUNKSGAARD. 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK. ISSN: 1600-5368. Pub. country: USA. Language: English.

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB The crystal and molecular structure of the title compound, C<sub>23</sub>H<sub>25</sub>NOS, has been determined by means of X-ray diffraction. This compound is readily lithiated with n-butyllithium at the 2-position of the thiophene ring to give a chiral lithiothiophene that can be used as a chiral template for enantioselective **conjugate** addition of an alkyl group to an enone.

L19 ANSWER 7 OF 161 MEDLINE on STN DUPLICATE 5

2003528238. PubMed ID: 14555291. In vivo characterization of bioconjugate B cell toleragens with specificity for autoantibodies in antiphospholipid syndrome. Cockerill Keith A; Smith Eric; Jones David S; Branks Michael J; Hayag Merle; Victoria Edward J; Linnik Matthew D; Campbell Mary-Ann. (La Jolla Pharmaceutical Company, 6455 Nancy Ridge Drive, San Diego, CA 92121, USA.. keith.cockerill@ljpc.com) . International immunopharmacology, (2003 Nov) 3 (12) 1667-75. Journal code: 100965259. ISSN: 1567-5769. Pub. country: Netherlands. Language: English.

AB This study investigated the use of well-defined bioconjugate molecules to suppress antigen-specific B cell responses to domain I (DI) of human beta(2)-glycoprotein I (beta(2)GPI) in rats. DI is the dominant target of pathogenic autoimmune antibodies in patients with antiphospholipid syndrome (APS), a disease characterized by antibody-mediated thromboembolic events. Rats primed with DI conjugated to keyhole limpet hemocyanin (DI-KLH) were rendered tolerant to subsequent antigen challenge by treatment with multivalent **conjugates** of DI. Antibodies to DI were suppressed 89-96% with intravenous doses of 500 micro g, and reductions were paralleled by decreases in splenic antigen-specific antibody-forming cells (AFC). Suppression was achieved with a variety of **conjugates** having two to four copies of DI and circulating half-lives of 2.6-8.7 h. Antibodies to KLH were not suppressed, indicating the specificity of the approach. These results establish the basis for further development of therapeutic B cell toleragens to suppress pathogenic antibodies in APS and other autoimmune diseases.

L19 ANSWER 8 OF 161 MEDLINE on STN

DUPLICATE 6

2003545703. PubMed ID: 14624619. Multivalent poly(ethylene glycol)-containing **conjugates** for in vivo antibody suppression. Jones David S; Branks Michael J; Campbell Mary-Ann; Cockerill Keith A; Hammaker Jeffrey R; Kessler Christina A; Smith Eric M; Tao Anping; Ton-Nu Huong-Thu; Xu Tong. (La Jolla Pharmaceutical Company, 6455 Nancy Ridge Drive, San Diego, California 92121, USA.. dave.jones@ljpc.com) . Bioconjugate chemistry, (2003 Nov-Dec) 14 (6) 1067-76. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB Poly(ethylene glycol) (PEG) was incorporated into multivalent **conjugates** of the N-terminal domain of beta(2)GPI (domain 1). PEG was incorporated to reduce the rate of elimination of the **conjugates** from plasma and to putatively improve their efficacy as toleragens for the suppression of anti-beta(2)GPI antibodies and the treatment of antiphospholipid syndrome (APS). Three structurally distinct types of multivalent platforms were constructed by incorporating PEG into the platform structures in different ways. The amount of PEG incorporated ranged from about 5000 g per mole to about 30000 g per mole. The platforms were functionalized with either four or eight aminooxy groups. The **conjugates** were prepared by forming oxime linkages between the aminooxy groups and N-terminally glyoxylated domain 1 polypeptide. The plasma half-life of each **conjugate**, labeled with (125)I, was measured in both mice and rats. The half-lives of the **conjugates** ranged from less than 10 min to about 1 h in mice, and from less than 3 h to about 19 h in rats. The ability of five tetravalent **conjugates** to suppress anti-domain 1 antibodies in immunized rats was also measured. Incorporation of PEG in the **conjugates** significantly reduced the doses required for suppression, and the amount of reduction correlated with the amount of PEG incorporated.

L19 ANSWER 9 OF 161 MEDLINE on STN DUPLICATE 7  
2003318446. PubMed ID: 12807356. Identification of novel electrophilic metabolites of piper methysticum Forst (Kava). Johnson Benjamin M; Qiu Sheng-Xiang; Zhang Shide; Zhang Fagen; Burdette Joanna E; Yu Linning; Bolton Judy L; van Breemen Richard B. (Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, University of Illinois at Chicago, 833 South Wood Street, Chicago, Illinois 60612-7231, USA. ) Chemical research in toxicology, (2003 Jun) 16 (6) 733-40. Journal code: 8807448. ISSN: 0893-228X. Pub. country: United States. Language: English.

AB Dietary supplements containing Piper methysticum Forst. (kava) have been implicated in multiple cases of liver injury in humans, including 10 recently reviewed cases in which patients required liver transplantation following the usage of kava-containing products (Centers for Disease Control and Prevention, reprinted. (2003) J. Am. Med. Associate 289, 36-37). To investigate a possible mechanism(s) of kava-induced hepatotoxicity, an extract of kava was incubated in vitro with hepatic microsomes, NADPH, and GSH. Electrophilic intermediates that were generated via metabolic activation were trapped as GSH **conjugates** and removed from the protein mixture using ultrafiltration. Positive ion electrospray LC-MS/MS with precursor ion scanning was used for the selective detection of GSH **conjugates**, and LC-MS(n) product ion scanning was used to elucidate their structures. Using this in vitro MS-based screening assay, two novel electrophilic metabolites of kava, 11,12-dihydroxy-7,8-dihydrokavain-o-quinone and 11,12-dihydroxykavain-o-quinone, were identified. Mercapturic acids of these quinoid species were not detected in the urine of a human volunteer following ingestion of a dietary supplement that contained kava; instead, the corresponding catechols were metabolized extensively to glucuronic acid and sulfate **conjugates**. These observations indicate that quinoid metabolites, under most circumstances, are probably not formed in substantial quantities following the ingestion of moderate doses of kava. However, the formation of electrophilic quinoid metabolites by hepatic microsomes in vitro suggests that such metabolites might contribute to hepatotoxicity in humans when metabolic pathways are altered (e.g., because of a drug interaction, genetic difference in enzyme expression, etc.) or if

conjugation pathways become saturated.

L19 ANSWER 10 OF 161 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

2004077601 EMBASE Iris melanocyte numbers in Asian, African American, and Caucasian irides. Albert D.M.; Green W.R.; Zimbric M.L.; Lo C.; Gangnon R.E.; Hope K.L.; Gleiser J.; Crawford J.B.; Spaeth G.L.; Eagle R.C.; Ing M.R.; **Jones D.B.** Dr. D.M. Albert, Dept. of Ophthalmol. and Vis. Sci., University of Wisconsin, Madison, WI, United States. Transactions of the American Ophthalmological Society 101/- (217-222) 2003. ISSN: 0065-9533. CODEN: TAOSAT. Pub. Country: United States. Language: English. Summary Language: English.

AB Purpose: The anatomical basis for iris color has long been a controversial issue in ophthalmology. Recent studies demonstrated that in Caucasians, blue-eyed, gray-eyed, and hazel-eyed individuals have comparable numbers of iris melanocytes. The present investigation was carried out to compare melanocyte numbers in the irides of Asian, African American, and Caucasian brown-eyed individuals. Methods: Paraffin-embedded sections from 71 brown-colored irides were incubated with rabbit anti-cow antibody against S100a, linked with an FITC **conjugate** antibody, and counterstained with Evans blue. Cells were counted under a fluorescence microscope and scored as melanocytes or other cells. Cell number, density, and iris area were calculated for each specimen. Results: Caucasian and African American irides had comparable mean total melanocyte numbers. Asian irides had fewer total melanocytes than African American ( $P = .042$ ) and Caucasian ( $P = .001$ ) irides and smaller total number of cells (ie, melanocytes plus other cells) than African American ( $P = .054$ ) or Caucasian ( $P = .009$ ) irides. Conclusions: There is a statistically significant smaller mean total melanocyte number and mean total cellularity in Asian irides as compared to Caucasian and African American irides. This difference appears to be due to the combination of smaller iris area and lower melanocyte density in the Asian irides. The possibility exists that this may be a factor in ethnic variations in certain ocular diseases.

L19 ANSWER 11 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
2003:637661 Metabolism of the SERM desmethylated arzoxifene to quinoids. Liu, Hong; Yang, Yanan; **Yu, Linning**; Van Breenman, Richard B.; Thatcher, Gregory R. J.; Bolton, Judy L. (Department of Medicinal Chemistry & Pharmacognosy, University of Illinois at Chicago, College of Pharmacy, Chicago, IL, 60612, USA). Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003, TOXI-085. American Chemical Society: Washington, D. C. (English) 2003. CODEN: 69EKY9.

AB Selective estrogen receptor modulators (SERMs), such as tamoxifen, are playing very important roles in the treatment and prevention of breast cancer. However, tamoxifen has been associated with an increased risk of endometrial cancer possibly due to metabolism to electrophilic quinoids. The SERM, arzoxifene is currently in clin. trials against breast cancer, it is critical to explore potential cytotoxic mechanisms of arzoxifene. In this study, the active form of arzoxifene in vivo, desmethylated arzoxifene (DMA), was synthesized and further oxidized to DMA quinone methide. The half-life of DMA quinone methide under physiol. conditions was approx. 15 s. The DMA quinone methide is therefore considerably more reactive than that from 4-hydroxytamoxifen. LC-MS/MS and NMR anal. showed that DMA quinone methide reacted with GSH to give GSH **conjugates**. In addition, enzymic oxidation of DMA in the presence of GSH gave DMA quinone methide and o-quinone GSH **conjugates**. These preliminary results suggest that DMA could be metabolized to electrophilic quinoids which have the potential to cause toxicity in vivo. Supported by NIH grant # CA 798700.

L19 ANSWER 12 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
2002:609797 Document No.: PREV200200609797. Valency platform molecules comprising carbamate linkages. **Jones, David S.** [Inventor,

Reprint author]. San Diego, CA, USA. ASSIGNEE: La Jolla Pharmaceutical Company. Patent Info.: US 6458953 October 01, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 1, 2002) Vol. 1263, No. 1. <http://www.uspto.gov/web/menu/patdata.html>. e-file. CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB This invention pertains generally to valency molecules, such as valency platform molecules which act as scaffolds to which one or more molecules may be covalently tethered to form a **conjugate**. More particularly, the present invention pertains to valency platform molecules which comprise a carbamate linkage (i.e., --O--C(dbdO)--Nlt;). In one aspect, the present invention pertains to valency platforms comprising carbamate linkages, which molecules have the structure of any one of Formulae I, II, or III, shown in FIG. 1. In one aspect, the present invention pertains to valency platforms comprising carbamate linkages, which molecules have the structure of any one of Formulae IV, V, or VI, shown in FIG. 8. The present invention also pertains to methods of preparing such valency platform molecules, **conjugates** comprising such valency platform molecules, and methods of preparing such **conjugates**.

L19 ANSWER 13 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN 2002:423913 Document No.: PREV200200423913. APL immunoreactive peptides, **conjugates** thereof and methods of treatment for APL antibody-mediated pathologies. Victoria, Edward Jess [Inventor, Reprint author]; Marquis, David Matthew [Inventor]; Jones, David S. [Inventor]; Yu, Lin [Inventor]. San Diego, CA, USA. ASSIGNEE: La Jolla Pharmaceutical Company. Patent Info.: US 6410775 June 25, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (June 25, 2002) Vol. 1259, No. 4. <http://www.uspto.gov/web/menu/patdata.html>. e-file.

CODEN: OGUPE7. ISSN: 0098-1133. Language: English.  
AB aPL analogs that (a) bind specifically to B cells to which an aPL epitope binds and are disclosed. Optimized analogs lack T cell epitope(s) are useful as **conjugates** for treating APL antibody-mediated diseases. **Conjugates** comprising aPL analogs and nonimmunogenic valency platform molecules are provided as are novel nonimmunogenic valency platform molecules and linkers. Methods of preparing and identifying said analogs, methods of treatment using said analogs, methods and compositions for preparing **conjugates** of said analogs and diagnostic immunoassays for APL antibodies are disclosed.

L19 ANSWER 14 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN 2002:378035 Document No.: PREV200200378035. **Conjugates** comprising galactose alpha1,3 galactosyl epitopes and methods of using same. Jack, Richard M. [Inventor, Reprint author]; Jones, David S. [Inventor]; Yu, Lin [Inventor]. Del Mar, CA, USA. ASSIGNEE: La Jolla Pharmaceutical Company. Patent Info.: US 6399578 June 04, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (June 4, 2002) Vol. 1259, No. 1. <http://www.uspto.gov/web/menu/patdata.html>. e-file.

CODEN: OGUPE7. ISSN: 0098-1133. Language: English.  
AB This invention provides **conjugates** useful for xenotransplantation which comprise a galactose alpha1,3 galactosyl (alphaGal) epitope conjugated to a valency platform molecule, preferably a chemically defined valency platform molecule which allows precise valency. The invention also provides compositions comprising these **conjugates**, and methods (such as methods for inducing tolerance) using these **conjugates** and compositions.

L19 ANSWER 15 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN 2002:810619 Robust infrared countermeasure system and method. Pepper, David M.; Jones, Dennis C. (USA). U.S. Pat. Appl. Publ. US 20020153497 A1 20021024 (English). CODEN: USXXCO. APPLICATION: US 2001-837733 20010418.

AB A system and method for focusing electromagnetic energy on a moving

target. Generally, the inventive system sends a pilot beam to a target and analyzes a return wavefront to ascertain data with respect to any distortions and other phase and/or amplitude information in the wavefront. This information is then used to pre-distort an output beam by so that it is focused on the target by the intervening distortions. In an illustrative embodiment, the pilot beam is provided by a beacon laser mounted off-axis with respect to the output beam. The reflected wavefront is received through a gimbaled telescope. Energy received by the telescope is detected and processed to ascertain wavefront aberrations therein. This data is used to predistort a deformable mirror to create an output beam which is the phase **conjugate** of the received wavefront. In a first alternative embodiment, a nonlinear optical phase-**conjugate** mirror is employed to generate the required wavefront-reversed replica of the received wavefront. The system further includes an arrangement for modulating the output beam to confuse the target. In a second alternative embodiment, the system is adapted to examine atmospheric distortions of starlight to predistort the output beam. The alternative embodiment offers a faster response time and a lower susceptibility to detection.

- L19 ANSWER 16 OF 161 MEDLINE on STN DUPLICATE 8  
 2002644316. PubMed ID: 12403583. Determination of 4-hydroxy-3-methoxyphenylethylene glycol 4-sulfate in human urine using liquid chromatography-tandem mass spectrometry. Jacob Peyton 3rd; Wilson Margaret; Yu Lisa; Mendelson John; Jones Reese T. (Division of Clinical Pharmacology, San Francisco General Hospital Medical Center, University of California, 94110, USA.. peyton@itsa.ucsf.edu) . Analytical chemistry, (2002 Oct 15) 74 (20) 5290-6. Journal code: 0370536. ISSN: 0003-2700. Pub. country: United States. Language: English.
- AB A major metabolite of norepinephrine (NE) in brain is 4-hydroxy-3-methoxyphenylethylene glycol (MHPG). In many species, a large fraction of MHPG formed in brain is converted to the sulfate **conjugate**. Consequently, MHPG sulfate has been proposed as a biomarker for NE metabolism in the central nervous system. As part of the clinical trials of the monoamine oxidase inhibitor selegiline for treating cocaine addiction, we required a method for measuring urine concentrations of MHPG sulfate. Using a deuterium-labeled analogue as an internal standard, we developed a liquid chromatography-electrospray ionization tandem mass spectrometry (LC-MS/MS) method for determination of MHPG sulfate in human urine. Sample preparation involves simply diluting 50 microL of urine with 1 mL of ammonium formate buffer and adding the internal standard. The sample is centrifuged, the supernate is transferred to an autosampler vial, and 10 microL is injected into the LC-MS/MS system. Standard curves from 50 to 10,000 ng/mL are generated. Only one sample of 277 clinical samples analyzed had a concentration outside of this range. Precision (coefficient of variation) ranged from 1.9 to 9.7%, and accuracy ranged from 97 to 103% of expected values for controls prepared by spiking sulfatase-treated urine with MHPG sulfate.

- L19 ANSWER 17 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 2002:845986 Document No. 139:73841 An angiogenic, endothelial-cell-targeted polymeric gene carrier. Suh, Wonhee; Han, Sang-Oh; Yu, Lei; Kim, Sung Wan (Department of Pharmaceuticals and Pharmaceutical Chemistry, Center for Controlled Chemical Delivery, University of Utah, Salt Lake City, UT, 84112, USA). Molecular Therapy, 6(5), 664-672 (English) 2002. CODEN: MTOHCK. ISSN: 1525-0016. Publisher: Elsevier Science.
- AB Targeting is one of the primary considerations in designing a specific and efficient gene delivery system. Here, an angiogenic endothelial cell-targeted polymeric gene delivery carrier was developed by conjugating an  $\alpha\beta3/\alpha\beta5$  integrin-binding RGD peptide, ACDCRGDCFC, into the cationic polymer polyethyleneimine (PEI) via a hydrophilic poly(ethylene glycol) (PEG) spacer. The incorporation of PEG into PEI improved the poor physicochem. properties of PEI-DNA complexes. At a neutral charge ratio, DNA complexes with PEI were polydisperse and substantially aggregated, whereas DNA complexes with PEI-g-1PEG-RGD were

homogeneous with 100-200 nm effective diameter. Their surface charge was also significantly reduced due to the charge shielding effect of PEG. However, the extensive grafting of PEI with PEG was shown to inhibit the DNA condensation process, significantly decreasing transfection efficiency. In in vitro transfection expts. with angiogenic endothelial cells, PEI-g-1PEG-RGD showed an approx. fivefold increase in transfection efficiency over PEI, due to an integrin-mediated internalization pathway. PEI-g-1PEG-RGD also exhibited high specificity to angiogenic endothelial cells compared with normal endothelial cells, which was confirmed by in vitro transfection expts. with non-targeting PEI-g-1PEG-RAE in angiostatic endothelial cells.

L19 ANSWER 18 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

2002:775531 Multivalent scaffolds comprised of polyethylene glycol and **conjugates** thereof. **Jones, David S.**; Hammaker, Jeffrey R.; Kessler, Christina A.; Tao, Anping; Ton-Nu, Huong-Thu (R&D, La Jolla Pharmaceutical Company, San Diego, CA, 92121, USA). Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002, ORGN-381. American Chemical Society: Washington, D. C. (English) 2002. CODEN: 69CZPZ.

AB Polyethylene glycol-containing multivalent platforms, scaffolds of defined valence, were synthesized, and they were used to prepare structurally diverse multivalent bioconjugates to be used as B cell Toleragens-. Polyethylene glycol (PEG) of various mol. weight ranges was incorporated into the platforms in three structurally distinct variations. Terminal aminoxy groups were attached and used to prepare **conjugates** of the N-terminal domain of  $\beta$ 2GPI (domain 1) using site-specific oxime bond formation.

L19 ANSWER 19 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

2002:718017 The Genuine Article (R) Number: 583RM. Multivalent scaffolds comprised of polyethylene glycol and **conjugates** thereof.. **Jones D S (Reprint)**; Hammaker J R; Kessler C A; Tao A P; Ton-Nu H T. La Jolla Pharmaceut Co, R&D, San Diego, CA 92121 USA. ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY (18 AUG 2002) Vol. 224, Part 2, pp. U173-U173. MA 381-ORGN. Publisher: AMER CHEMICAL SOC. 1155 16TH ST, NW, WASHINGTON, DC 20036 USA. ISSN: 0065-7727. Pub. country: USA. Language: English.

L19 ANSWER 20 OF 161 MEDLINE on STN

DUPLICATE 9

2002087236. PubMed ID: 11815407. Metabolism of the cancer chemopreventive agent curcumin in human and rat intestine. Ireson Christopher R; **Jones Donald J L**; Orr Samantha; Coughtrie Michael W H; Boocock David J; Williams Marion L; Farmer Peter B; Steward William P; Gescher Andreas J. (Medical Research Council Toxicology Unit, University of Leicester, Leicester LE1 9HN, United Kingdom. ) Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology, (2002 Jan) 11 (1) 105-11. Journal code: 9200608. ISSN: 1055-9965. Pub. country: United States. Language: English.

AB Curcumin, the yellow pigment in turmeric, prevents malignancies in the intestinal tract of rodents. It is under clinical evaluation as a potential colon cancer chemopreventive agent. The systemic bioavailability of curcumin is low, perhaps attributable, at least in part, to metabolism. Indirect evidence suggests that curcumin is metabolized in the intestinal tract. To investigate this notion further, we explored curcumin metabolism in subcellular fractions of human and rat intestinal tissue, compared it with metabolism in the corresponding hepatic fractions, and studied curcumin metabolism in situ in intact rat intestinal sacs. Analysis by high-performance liquid chromatography, with detection at 420 or 280 nm, permitted characterization of curcumin **conjugates** and reduction products. Chromatographic inferences were corroborated by mass spectrometry. Curcumin glucuronide was identified in intestinal and hepatic microsomes, and curcumin sulfate, tetrahydrocurcumin, and hexahydrocurcumin were found as curcumin

metabolites in intestinal and hepatic cytosol from humans and rats. The extent of curcumin conjugation was much greater in intestinal fractions from humans than in those from rats, whereas curcumin conjugation was less extensive in hepatic fractions from humans than in those from rats. The curcumin-reducing ability of cytosol from human intestinal and liver tissue exceeded that observed with the corresponding rat tissue by factors of 18 and 5, respectively. Curcumin sulfate was identified in incubations of curcumin with intact rat gut sacs. Curcumin was sulfated by human phenol sulfotransferase isoenzymes SULT1A1 and SULT1A3. Equine alcohol dehydrogenase catalyzed the reduction of curcumin to hexahydrocurcumin. The results show that curcumin undergoes extensive metabolic conjugation and reduction in the gastrointestinal tract and that there is more metabolism in human than in rat intestinal tissue. The pharmacological implications of the intestinal metabolism of curcumin should be taken into account in the design of future chemoprevention trials of this dietary constituent.

L19 ANSWER 21 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

2002:779090 Formation and reactivity of a raloxifene quinone methide.

**Yu, Linning**; Zhang, Fagen; Nikolic, Dejan; Li, Wenkui; van Breemen, Richard B.; Bolton, Judy L. (Department of Medicinal Chemistry and Pharmacognosy, University of Illinois at Chicago, Chicago, IL, 60612, USA). Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002, TOXI-068. American Chemical Society: Washington, D. C. (English) 2002. CODEN: 69CZPZ.

AB Long-term usage of the antiestrogen tamoxifen has been linked to increased risk of developing endometrial cancer in women. One of the suggested pathways leading to toxicity of tamoxifen involves its metabolism to an electrophilic quinone methide which could attack cellular macromols. leading to initiation of carcinogenesis. Another antiestrogen raloxifene was recently approved by the FDA for treatment of osteoporosis in postmenopausal women and it is currently in clin. trials for chemoprevention of breast cancer. Before it is widely used for healthy individuals, it is crucial to fully understand its potential cytotoxic mechanisms since raloxifene has a similar structure to tamoxifen. In this study, incubations of raloxifene with GSH in the presence of rat liver microsomes or tyrosinase were carried out and analyzed by LC/MS-MS. The results showed that incubations with raloxifene formed GSH **conjugates** which were identified as the raloxifene quinone methide GSH **conjugates**. These preliminary results suggest that raloxifene could be metabolized to an electrophilic quinoid which has the potential to cause toxicity in vivo. (Supported by NIH grant CA79870).

L19 ANSWER 22 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

2002:521503 Document No.: PREV200200521503. Multivalent scaffolds comprised of polyethylene glycol and **conjugates** thereof. **Jones, David**

S. [Reprint author]; Hammaker, Jeffrey R. [Reprint author]; Kessler, Christina A. [Reprint author]; Tao, Anping [Reprint author]; Ton-Nu, Huong-Thu [Reprint author]. R and D, La Jolla Pharmaceutical Company, 6455 Nancy Ridge Drive, San Diego, CA, 92121, USA. dave.jones@ljpc.com.

Abstracts of Papers American Chemical Society, (2002) Vol. 224, No. 1-2, pp. ORGN 381. print.

Meeting Info.: 224th National Meeting of the American Chemical Society. Boston, MA, USA. August 18-22, 2002.

CODEN: ACSRAL. ISSN: 0065-7727. Language: English.

L19 ANSWER 23 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

2001:903935 Document No. 136:54229 Multivalent platform molecules comprising high molecular weight polyethylene oxide. **Jones, David S.** (La

Jolla Pharmaceutical Company, USA). PCT Int. Appl. WO 2001093914 A2 20011213, 78 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,



UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US18446 20010607. PRIORITY: US 2000-PV210439 20000608.

AB Valency platform mols. comprising high mol. weight polyethylene oxide groups are provided, as well as **conjugates** with biol. active mols., and methods for their preparation. The high mol. weight polyethylene oxide group

has

mol. weight at least 40,000 Daltons. In one embodiment, a composition comprising

the valency platform mols. is provided, wherein the mols. have a polydispersity less than about 1.2. **Conjugates** of the valency platform mol. and a biol. active mol., such as a saccharide, poly(saccharide), amino acid, poly(amino acid), nucleic acid or lipid also are provided. Also provided are pharmaceutically acceptable compns. comprising the **conjugates** disclosed herein and a pharmaceutically acceptable carrier, as well as methods of making and using the **conjugates** and compns.

L19 ANSWER 24 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
2001:224355 Document No. 134:265135 B-cell tolerogens for treatment for pathologies mediated by antibodies to phospholipids. Victoria, Edward Jess; Marquis, David Matthew; Jones, David S.; Yu, Lin (La Jolla Pharmaceutical Company, USA). U.S. US 6207160 B1 20010327, 113 pp., Cont.-in-part of U.S. 5,874,409. (English). CODEN: USXXAM. APPLICATION: US 1996-660092 19960606. PRIORITY: US 1995-482651 19950607.

AB The authors disclose analogs of anti-phospholipid antibody (aPL) epitopes that (a) bind specifically to B cells to and (b) do not induce T-cell activation. In addition, the authors disclose the preparation of

non-immunogenic

tetravalent scaffolds to which the synthetic tolerogens can be attached.

L19 ANSWER 25 OF 161 MEDLINE on STN DUPLICATE 10  
2001697917. PubMed ID: 11743747. Synthesis and reactivity of potential toxic metabolites of tamoxifen analogues: droloxifene and toremifene o-quinones. Yao D; Zhang F; Yu L; Yang Y; van Breemen R B; Bolton J L. (Department of Medicinal Chemistry and Pharmacognosy (M/C 781), College of Pharmacy, University of Illinois at Chicago, 833 South Wood Street, Chicago, Illinois 60612-7231, USA. ) Chemical research in toxicology, (2001 Dec) 14 (12) 1643-53. Journal code: 8807448. ISSN: 0893-228X. Pub. country: United States. Language: English.

AB Tamoxifen remains the endocrine therapy of choice in the treatment of all stages of hormone-dependent breast cancer. However, tamoxifen has been shown to increase the risk of endometrial cancer which has stimulated research for new effective antiestrogens, such as droloxifene and toremifene. In this study, the potential for these compounds to cause cytotoxic effects was investigated. One potential cytotoxic mechanism could involve metabolism of droloxifene and toremifene to catechols, followed by oxidation to reactive o-quinones. Another cytotoxic pathway could involve the oxidation of 4-hydroxytoremifene to an electrophilic quinone methide. Comparison of the amounts of GSH **conjugates** formed from 4-hydroxytamoxifen, droloxifene, and 4-hydroxytoremifene suggested that 4-hydroxytoremifene is more effective at formation of a quinone methide. However, all three substrates formed similar amounts of o-quinones. Both the tamoxifen-o-quinone and toremifene-o-quinone reacted with deoxynucleosides to give corresponding adducts. However, the toremifene-o-quinone was shown to be considerably more reactive than the tamoxifen-o-quinone in terms of both kinetic data as well as the yield and type of deoxynucleoside adducts formed. Since thymidine formed the most abundant adducts with the toremifene-o-quinone, sufficient material was obtained for characterization by (1)H NMR, COSY-NMR, DEPT-NMR, and tandem mass spectrometry. Cytotoxicity studies with tamoxifen, droloxifene, 4-hydroxytamoxifen, 4-hydroxytoremifene, and their catechol metabolites were carried out in the human breast cancer cell lines S30 and MDA-MB-231.



All of the metabolites tested showed cytotoxic effects that were similar to the parent antiestrogens which suggests that o-quinone formation from tamoxifen, droloxifene, and 4-hydroxytoremifene is unlikely to contribute to their cytotoxicity. However, the fact that the o-quinones formed adducts with deoxynucleosides in vitro implies that the o-quinone pathway might contribute to the genotoxicity of the antiestrogens in vivo.

L19 ANSWER 26 OF 161 MEDLINE on STN DUPLICATE 11  
2001671159. PubMed ID: 11716694. Synthesis of LJP 993, a multivalent **conjugate** of the N-terminal domain of beta2GPI and suppression of an anti-beta2GPI immune response. Jones D S; Cockerill K A; Gamino C A; Hammaker J R; Hayag M S; Iverson G M; Linnik M D; McNeeley P A; Tedder M E; Ton-Nu H T; Victoria E J. (La Jolla Pharmaceutical Company, 6455 Nancy Ridge Drive, San Diego, California 92121, USA.. dave.jones@ljpc.com) . Bioconjugate chemistry, (2001 Nov-Dec) 12 (6) 1012-20. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB LJP 993, a tetravalent **conjugate** of the amino-terminal domain (domain 1) of beta2GPI, was synthesized, and studies were carried out to explore the ability of LJP 993 to bind anti-beta2GPI antibodies and to function as a B cell toleragen. Domain 1 was expressed in *Pichia pastoris*, and the N-terminus was site-specifically modified by a transamination reaction converting the N-terminal glycine to a glyoxyl group. A tetravalent platform was synthesized with linkers that terminate in aminooxy groups. This was accomplished by preparing an ethylene glycol-based heterobifunctional linker that contains both a Boc-protected aminooxy group and a free primary amine. The linker was used to modify a tetravalent platform molecule by reacting the amino groups on the linker with 4-nitrophenyl carbonate esters on the platform to provide a linker-modified platform, and the Boc protecting groups were removed to provide a tetravalent aminooxy platform. Glyoxylated domain 1 was attached to the platform to provide LJP 993 by formation of oxime bonds. The protein domains of LJP 993 retain activity as evidenced by the ability of LJP 993 to bind to anti-beta2GPI antibodies. Dissociation constants (Kd) for domain 1 and LJP 993 bound to immobilized affinity-purified anti-beta2GPI antibodies from autoimmune thrombosis patients were determined using surface plasmon resonance. An immunized mouse model was developed to test the ability of LJP 993 to act as a toleragen. A thiol containing domain 1 analogue was expressed in insect cells using the baculovirus expression system, and it was used to prepare an immunogenic **conjugate** of domain 1 and maleimide-derivatized keyhole limpet hemocyanin (KLH). Mice were immunized with the KLH **conjugate**, and spleen cells were harvested from the immunized mice. The cells were incubated with various concentrations of LJP 993 and transferred to mice whose immune systems had been compromised by irradiation. The hosts were then boosted with the KLH-domain 1 **conjugate**, and after 7 days their antibody levels were measured. Host mice receiving cells that were treated with LJP 993 produced significantly lower amounts of anti-domain 1 antibodies than controls which received untreated cells, indicative of B cell tolerance.

L19 ANSWER 27 OF 161 MEDLINE on STN DUPLICATE 12  
2002024461. PubMed ID: 11480552. Biostability and pharmacokinetics of LJP 920, an octameric Gal (alpha1-3) Gal **conjugate** for the inhibition of xenotransplantation rejection. Jia L; Linnik M D; Jack R M; Yu L. (La Jolla Pharmaceutical Company, San Diego, CA 92121, USA.. Ljia@saci.org) . Journal of pharmacy and pharmacology, (2001 Jul) 53 (7) 999-1005. Journal code: 0376363. ISSN: 0022-3573. Pub. country: England: United Kingdom. Language: English.

AB Antibodies to an alpha-galactosyl saccharide structure present in human serum are associated with hyperacute rejection and delayed xenograft rejection after pig-to-primate xenotransplantation. To overcome this major barrier to the xenotransplantation, LJP 920, a galactosyl alpha1-3 galactose (Gal (alpha1-3) Gal) coupled to a non-immunogenic platform at a valency of eight Gal (alpha1-3) Gal molecules/platform, was synthesized to

clear circulating antibodies and to inhibit their production by B cells that produce these antibodies. Herein we report on the stability of UP 920 in biological media and its pharmacokinetic profile. Incubation of LJP 920 with mouse serum or liver microsomes at 37 degrees C for 2 days showed no indication of degradation of the **conjugate** as detected by a reversed-phase HPLC method, indicating that the **conjugate** is not subject to enzymatic metabolism. After intravenous administration of LJP 920 to mice at the doses of 20 and 100 mg kg<sup>-1</sup>, UP 920 serum concentration decreased rapidly, showing a biphasic pattern, with a distribution half-life of 3 min and an elimination half-life of more than 30 min, respectively. The serum-to-erythrocyte concentration ratio of UP 920 was 33- and 36-fold excess at 0.5 and 5 min, respectively, after intravenous administration (100 mg kg<sup>-1</sup>). Both C<sub>max</sub> and AUC values increased in a dose-proportional manner. UP 920 displayed a great distribution to well-perfused tissues. It was eliminated mainly through renal excretion in the unchanged form, which accounted for 23% of the total amount within 8 h of dosing.

- L19 ANSWER 28 OF 161 MEDLINE on STN DUPLICATE 13  
 2002023208. PubMed ID: 11453733. Serotonergic neurotoxicity of 3,4-(+/-)-methylenedioxyamphetamine and 3,4-(+/-)-methylenedioxymethamphetamine (ecstasy) is potentiated by inhibition of gamma-glutamyl transpeptidase. Bai F; Jones D C; Lau S S; Monks T J. (Center for Cellular and Molecular Toxicology, College of Pharmacy, University of Texas at Austin, Austin, Texas 78712-1074, USA. ) Chemical research in toxicology, (2001 Jul) 14 (7) 863-70. Journal code: 8807448. ISSN: 0893-228X. Pub. country: United States. Language: English.
- AB Reactive metabolites play an important role in 3,4-(+/-)-methylenedioxyamphetamine (MDA) and 3,4-(+/-)-methylenedioxymethamphetamine (MDMA; ecstasy)-mediated serotonergic neurotoxicity, although the specific identity of such metabolites remains unclear. 5-(Glutathion-S-yl)-alpha-methyldopamine (5-GSyl-alpha-MeDA) is a serotonergic neurotoxicant found in the bile of MDA-treated rats. The brain uptake of 5-GSyl-alpha-MeDA is decreased by glutathione (GSH), but sharply increases in animals pretreated with acivicin, an inhibitor of gamma-glutamyl transpeptidase (gamma-GT) suggesting competition between intact 5-GSyl-alpha-MeDA and GSH for the putative GSH transporter. gamma-GT is enriched in blood-brain barrier endothelial cells and is the only enzyme known to cleave the gamma-glutamyl bond of GSH. We now show that pretreatment of rats with acivicin (18 mg/kg, ip) inhibits brain microvessel endothelial gamma-GT activity by 60%, and potentiates MDA- and MDMA-mediated depletions in serotonin (5-HT) and 5-hydroxyindole acidic acid (5-HIAA) concentrations in brain regions enriched in 5-HT nerve terminal axons (striatum, cortex, hippocampus, and hypothalamus). In addition, glial fibrillary acidic protein (GFAP) expression increases in the striatum of acivicin and MDA (10 mg/kg) treated rats, but remains unchanged in animals treated with just MDA (10 mg/kg). Inhibition of endothelial cell gamma-GT at the blood-brain barrier likely enhances the uptake into brain of thioether metabolites of MDA and MDMA, such as 5-(glutathion-S-yl)-alpha-MeDA and 2,5-bis-(glutathion-S-yl)-alpha-MeDA, by increasing the pool of thioether **conjugates** available for uptake via the intact GSH transporter. The data indicate that thioether metabolites of MDA and MDMA contribute to the serotonergic neurotoxicity observed following peripheral administration of these drugs.

- L19 ANSWER 29 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 2002:174820 Document No. 137:121649 Preparation of anti bladder cancer monoclonal antibody BDI-1 labeled with rhenium-188. Wang, Rongfu; Zhang, Chungli; Yu, Lizhang; Guo, Yifeng; Bai, Ying (Department of Nuclear Medicine, Peking University First Hospital, Beijing, 100034, Peop. Rep. China). Synthesis and Applications of Isotopically Labelled Compounds, Proceedings of the International Symposium, 7th, Dresden, Germany, June 18-22, 2000, Meeting Date 2000, 400-403. Editor(s): Pleiss, Ulrich; Voges, Rolf. John Wiley & Sons Ltd.: Chichester, UK. ISBN: 0-471-49501-8 (English) 2001. CODEN: 69CIJC.

AB Anti-bladder tumor monoclonal antibody BDI-1 labeled with radionuclide rhenium-188 (188Re-BDI-1) was prepared by indirect method with 188Re-NHS-ECM and direct 2-mercaptoethanol-reduction method. A higher labeling yield was obtained from indirect method (87.4%) compared with the direct method (30%). The immunoreactive fraction of 188Re-BDI-1 was > 58.7% and the radiochem. purity of both methods was > 95%. The results justifies the development of radioimmunoconjugates for radioimmunotherapy and particularly provides a novel means for radionuclide intraradiation therapy of bladder cancer by intravesical perfusion of 188Re-BDI-1.

L19 ANSWER 30 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

2001:202775 Site-specific attachment of a protein to a multivalent platform: Synthesis of LJP 993, a tetravalent protein **conjugate**.  
**Jones, David S.**; Cockerill, Keith A.; Gamino, Christina A.; Hammaker, Jeffrey R.; Ton-Nu, Huong-Thu (R&D, La Jolla Pharmaceutical Company, San Diego, CA, 92121, USA). Abstracts of Papers - American Chemical Society, 221st, ORGN-281 (English) 2001. CODEN: ACSRAL. ISSN: 0065-7727. Publisher: American Chemical Society.

AB A chemical defined tetravalent protein **conjugate**, LJP 993, was synthesized for testing as a B cell toleragen for the treatment of autoimmune thrombosis. The first domain of the five domain protein, b2GPI, expressed in *Pichia pastoris*, was site specifically modified by a transamination reaction to provide a glyoxyl group at the N-terminus. A six carbon heterobifunctional linker was prepared which contains a Boc-protected aminooxy group and a free primary amine. The linker was reacted with a tetravalent activated carbonate ester intermediate to provide a tetravalent platform with four Boc-protected aminooxy groups. The protecting groups were removed, and the transaminated protein was attached to the resultant aminooxy groups to provide a tetravalent protein **conjugate** by formation of oxime bonds.

L19 ANSWER 31 OF 161 MEDLINE on STN

DUPLICATE 14

2001:152014. PubMed ID: 11162782. Role of mitochondrial dysfunction in S-(1,2-dichlorovinyl)-l-cysteine-induced apoptosis. Chen Y; Cai J; Anders M W; Stevens J L; **Jones D P.** (Program of Biochemistry, Cell Biology and Developmental Biology, Emory University, Atlanta, Georgia 30322, USA. ) Toxicology and applied pharmacology, (2001 Feb 1) 170 (3) 172-80. Journal code: 0416575. ISSN: 0041-008X. Pub. country: United States. Language: English.

AB The nephrotoxicity of trichloroethylene and dichloroacetylene has previously been linked to mitochondrial dysfunction induced by the metabolite S-(1,2-dichlorovinyl)-l-cysteine (DCVC). In this study, we examined whether key biochemical steps associated with mitochondria occur in DCVC-induced apoptosis in cultured porcine proximal tubular LLC-PK1 cells. DCVC caused a decrease in mitochondrial membrane potential (mt Delta Psi) beginning at 4 h and a release of cytochrome c into the cytoplasm at 6 h. Caspase-3-like activity was detected at 6 h and extensive DNA fragmentation was observed at 8 h. Decreases in cellular ATP were not evident until 8 h and later, even though electron microscopy showed that the mitochondria were extensively swollen. Aminooxyacetic acid (AOAA), an inhibitor of cysteine-**conjugate** beta-lyase, protected against mitochondrial changes and apoptosis. Overexpression of the antiapoptotic Bcl-2 protein desensitized LLC-PK1 cells to DCVC-induced apoptosis. These results support the interpretation that mitochondrial release of cyt c and cyt c-dependent activation of caspase-3 could have a central role in nephrotoxicity due to haloalkene-derived cysteine S-**conjugates**.

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L19 ANSWER 32 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

2001:659154 The Genuine Article (R) Number: 434PJ. Site-specific attachment of a protein to a multivalent platform: Synthesis of LJP 993, a tetravalent protein **conjugate**. **Jones D S (Reprint)**; Cockerill K A; Gamino C A; Hammaker J R; Ton-Nu H T. La Jolla Pharmaceut Co, R&D, San Diego, CA 92121 USA. ABSTRACTS OF PAPERS OF THE AMERICAN

CHEMICAL SOCIETY (1 APR 2001) Vol. 221, Part 2, pp. U150-U150. MA 281-ORGN  
. Publisher: AMER CHEMICAL SOC. 1155 16TH ST, NW, WASHINGTON, DC 20036 USA  
. ISSN: 0065-7727. Pub. country: USA. Language: English.

L19 ANSWER 33 OF 161 MEDLINE on STN

2001485089. PubMed ID: 11527012. Tetracel (American Home Products).

**Jones D H.** (Intellivax International Inc, Ville St-Laurent, Quebec, Canada.. [tjones@intellivax.com](mailto:tjones@intellivax.com)) . Current opinion in investigational drugs (London, England : 2000), (2001 Jan) 2 (1) 50-2. Journal code: 100965718. ISSN: 1472-4472. Pub. country: England: United Kingdom. Language: English.

AB American Home Products (AHP) is developing Tetracel as a vaccine for children (aged 12 to 18 months) against diphtheria, tetanus, pertussis and Haemophilus influenzae type B (Hib) [275146]. The components are contained in AHP's two currently marketed vaccines. ACEL-Immune contains diphtheria and tetanus toxoids with acellular pertussis vaccine adsorbed, and HibTITER contains the Haemophilus influenzae B **conjugate** vaccine (diphtheria CRM197 protein **conjugate**) [239655]. As of January 2000, Lehman Brothers predicted Tetracel to be approved in the US during 2000 [354434].

L19 ANSWER 34 OF 161 MEDLINE on STN

2001485088. PubMed ID: 11527011. Menjugate (Chiron). **Jones D H.** (Intellivax International Inc, Ville St-Laurent, Quebec, Canada.. [tjones@intellivax.com](mailto:tjones@intellivax.com)) . Current opinion in investigational drugs (London, England : 2000), (2001 Jan) 2 (1) 47-9. Journal code: 100965718. ISSN: 1472-4472. Pub. country: England: United Kingdom. Language: English.

AB Chiron has developed and launched Menjugate, a vaccine for the treatment for meningococcus C infections caused by the pathogen Neisseria meningitidis [177064]. In August 1999, Chiron filed with the UK MCA for a license to market Menjugate. The licence was granted in March 2000 [339082], [344773], [357897] and as of April 2000, a vaccination program was underway in the UK [362152]. Menjugate is indicated for children of 12 months and older, but Chiron was expecting approval in the US for infants younger than 12 months by the end of 2000. The company will also pursue mutual recognition in Europe [376204]. In August 2000, Chiron received marketing clearance for Menjugate from the Irish Medicines Board as a **conjugate** against meningococcal C disease [378353]. The vaccine employs CRM-**conjugate** technology, whereby a diphtheria toxoid is used as a carrier protein for the meningitis C-specific antigens. The vaccine is being developed for its potential to provide protection against meningitis in both adults and infants. In July 2000, Chiron entered into a comarketing and co-promotion agreement with Aventis Pasteur under which Aventis will assist Chiron in marketing and sales efforts for Menjugate in the UK [374760].

L19 ANSWER 35 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

2001:333852 Document No.: PREV200100333852. Site-specific attachment of a protein to a multivalent platform: Synthesis of LJP 993, a tetravalent protein **conjugate**. **Jones, David S.** [Reprint author]; Cockerill, Keith A. [Reprint author]; Gamino, Christina A. [Reprint author]; Hammaker, Jeffrey R. [Reprint author]; Ton-Nu, Huong-Thu [Reprint author]. R and D, La Jolla Pharmaceutical Company, 6455 Nancy Ridge Drive, San Diego, CA, 92121, USA. [dave.jones@ljpc.com](mailto:dave.jones@ljpc.com). Abstracts of Papers American Chemical Society, (2001) Vol. 221, No. 1-2, pp. ORGN 281. print. Meeting Info.: 221st National Meeting of the American Chemical Society. San Diego, California, USA. April 01-05, 2001. American Chemical Society. CODEN: ACSRAL. ISSN: 0065-7727. Language: English.

L19 ANSWER 36 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

2000:881116 Document No. 134:56426 Preparation of molecules containing aminoxy groups as valency platform molecules for preparation of bioconjugates.. **Jones, David S.**; Ton-nu, Huong-thu; Xie, Fang; Tao, Anping; Xu, Tong; Hammaker, Jeffrey Robert (La Jolla Pharmaceutical Co., USA). PCT Int. Appl. WO 2000075105 A1 20001214, 113 pp. DESIGNATED

STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US15968 20000608.

PRIORITY: US 1999-PV138260 19990608.

AB Oxyalkylene mols. containing  $\geq 3$  aminoxy groups were prepared Thus,  $\text{MeO}(\text{CH}_2\text{CH}_2\text{O})_n\text{CH}_2\text{CH}_2\text{O}_2\text{CN}[\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{O}_2\text{CN}[\text{CH}_2\text{CH}_2\text{NHCO}(\text{CH}_2)_5\text{NHCO}(\text{CH}_2)_5\text{NH}_2]_2]_2$  ( $n = \text{approx. } 503$ ) (preparation outlined) was stirred with Domain 1 polypeptide  $\beta 2\text{GPI}$ -glyoxylic acid reaction product to give the tetraadduct, which at  $0.17 \text{ nmol/rat}$  gave  $61\%$  suppression of anti-Domain 1 antibody in immunized rats.

L19 ANSWER 37 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

2000:401844 Document No. 133:42177 **Conjugates** comprising galactose alpha 1,3 galactosyl epitopes and methods of using same. Jack, Richard M.; Jones, David; Yu, Lin (La Jolla Pharmaceutical Company, USA). PCT Int. Appl. WO 2000034296 A2 20000615, 100 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US29338 19991209. PRIORITY: US 1998-PV111644 19981209; US 1999-PV160997 19991023; US 1999-457913 19991208.

AB This invention provides **conjugates** useful for xenotransplantation which comprise a galactose  $\alpha 1,3$  galactosyl ( $\alpha\text{Gal}$ ) epitope conjugated to a valency platform mol., preferably a chemical defined valency platform mol. which allows precise valency. The invention also provides compns. comprising these **conjugates**, and methods (such as methods for inducing tolerance) using these **conjugates** and compns.

L19 ANSWER 38 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

2000:401781 Document No. 133:44002 Dendritic molecular scaffolds acting as templates comprising carbamate linkages. Jones, David S. (La Jolla Pharmaceutical Company, USA). PCT Int. Appl. WO 2000034231 A1 20000615, 127 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US29339 19991209. PRIORITY: US 1998-PV111641 19981209; US 1999-457607 19991208.

AB This invention pertains generally to valency mols., such as valency platform mols. which act as scaffolds to which one or more mols. may be covalently tethered to form a **conjugate**. More particularly, the present invention pertains to valency platform mols. which comprise a carbamate linkage (i.e.,  $-\text{O}-\text{C}(=\text{O})-\text{N}<$ ). The present invention also pertains to methods of preparing such valency platform mols., **conjugates** comprising such valency platform mols., and methods of preparing such **conjugates**.

L19 ANSWER 39 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

2000:401689 Document No. 133:38230 Methods and formulations based on epitope-presenting carriers for reducing circulating antibodies. Jack, Richard M.; Jones, David S.; Yu, Lin; Engle, Steven B.

(La Jolla Pharmaceutical Company, USA). PCT Int. Appl. WO 2000033887 A2 20000615, 74 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US29336 19991209. PRIORITY: US 1998-PV111639 19981209; US 1999-457875 19991208.

AB The invention provides methods for reducing circulating levels of antibodies, particularly disease-associated antibodies. The methods entail administering effective amts. of epitope-presenting carriers to an individual. In other embodiments, ex vivo methods for reducing circulating levels of antibodies are provided which employ epitope-presenting carriers. For example, an octameric toleragen LJP 920 was prepared and used for treating two rhesus monkeys i.v. at a dose of 20 mg/kg daily for 7 days. At day 8, IgG anti- $\alpha$ Gal levels were decreased by 11%, while control animals showed little change. Similarly, there was a diminution of 18% in IgM anti- $\alpha$ Gal levels in one monkey and 5% in the replicate animal. By contrast, IgM anti- $\alpha$ Gal levels in the control animals did not change in one animal and increased in the replicate animal. The octamer was more efficient than the tetramer LJP 712 at clearing IgM anti- $\alpha$ Gal, indicating that increased valency results in a more efficacious mol.

L19 ANSWER 40 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
2000:307077 Document No. 132:320935 Induction of humoral anergy using immunogen **conjugates** lacking T-cell epitopes. **Coutts, Stephen M.**; Barstad, Paul A.; Iverson, G. Michael; **Jones, David S.** (La Jolla Pharmaceutical Company, USA). U.S. US 6060056 A 20000509, 30 pp., Cont.-in-part of U.S. 5,268,454. (English). CODEN: USXXAM. APPLICATION: US 1993-118055 19930908. PRIORITY: US 1991-652648 19910208.

AB The authors disclose the preparation of **conjugates** of non-immunogenic carrier mols. with B-cell epitopes that possess ability to suppress antigen-specific antibody responses. In one example, mice were primed with the main immunogenic region of the acetylcholine receptor. Subsequent immunization of these mice with a B-cell epitope peptide, lacking the ability to activate primed T-cells, led to a specific suppression of the anti-receptor antibody response. In a second example, mice were primed with the bee venom allergen, mellitin. Immunization with peptides conjugated to lysine-glutamate copolymer suppressed the anti-mellitin response.

L19 ANSWER 41 OF 161 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN  
2000202000 EMBASE Phase I trial of the anti-Lewis Y drug immunoconjugate BR96-doxorubicin in patients with Lewis Y-expressing epithelial tumors. Saleh M.N.; Sugarman S.; Murray J.; Ostroff J.B.; Healey D.; **Jones D.**; Daniel C.R.; LeBherz D.; Brewer H.; Onetto N.; LoBuglio A.F.. Dr. M.N. Saleh, Department of Medicine, Wallace Tumor Institute 223, University of Alabama, 1824 Sixth Ave South, Birmingham, AL 35294-3300, United States. mansoor.saleh@ccc.uab.edu. Journal of Clinical Oncology 18/11 (2282-2292) 2000.  
Refs: 27.

ISSN: 0732-183X. CODEN: JCONDN. Pub. Country: United States. Language: English. Summary Language: English.  
AB Purpose: We conducted a phase I clinical trial of BR96-Doxorubicin (BR96-Dox), a chimeric anti-Lewis Y (Le(Y)) monoclonal antibody conjugated to doxorubicin, in patients whose tumors expressed the Le(Y) antigen. The study aimed to determine the toxicity, maximum-tolerated dose, pharmacokinetics, and immunogenicity of BR96-Dox. Patients and Methods: This was a phase I dose escalation study. BR96-Dox was initially administered alone as a 2-hour infusion every 3 weeks. The occurrence of

gastrointestinal (GI) toxicity necessitated the administration of BR96-Dox as a continuous infusion over 24 hours and use of antiemetics and antigastritis premedication. Patients experiencing severe GI toxicity underwent GI endoscopy. All patients underwent restaging after two cycles. Results: A total of 66 patients predominantly with metastatic colon and breast cancer were enrolled onto the study. The most common side effects were GI toxicity, fever, and elevation of pancreatic lipase. At higher doses, BR96-Dox was associated with nausea, vomiting, and endoscopically documented exudative gastritis of the upper GI tract, which was dose-limiting at a maximum dose of 875 mg/m<sup>2</sup> (doxorubicin equivalent, 25 mg/m<sup>2</sup>) administered every 3 weeks. Toxicity was reversible and generally of short duration. Premedication with the antiemetic Kytril (granisetron hydrochloride; SmithKline Beecham, Philadelphia, PA), the antacid omeprazole, and dexamethasone was most effective in ameliorating GI toxicity. A dose of 700 mg/m<sup>2</sup> BR96-Dox (doxorubicin equivalent, 19 mg/m<sup>2</sup>) every 3 weeks was determined to be the optimal phase II dose when administered with antiemetic and antigastritis prophylaxis. BR96-Dox deposition on tumor tissue was documented immunohistochemically and by confocal microscopy. At the 550-mg/m<sup>2</sup> dose, the half-life (mean  $\pm$  SD) of BR96 and doxorubicin was 300  $\pm$  95 hours and 43  $\pm$  4 hours, respectively. BR96-Dox elicited a weak immune response in 37% of patients. Objective clinical responses were seen in two patients. Conclusion: BR96-Dox provides a unique strategy to deliver doxorubicin to Le(Y)-expressing tumor and was well tolerated at doses of 700 mg/m<sup>2</sup> every 3 weeks. BR96-Dox was not associated with the typical side-effect profile of native doxorubicin and can potentially deliver high doses of doxorubicin to antigen-expressing tumors. A phase II study in doxorubicin-sensitive tumors is warranted. (C) 2000 by American Society of Clinical Oncology.

- L19 ANSWER 42 OF 161 MEDLINE on STN DUPLICATE 16  
 2001020999. PubMed ID: 10993680. The NED-8 conjugating system in *Caenorhabditis elegans* is required for embryogenesis and terminal differentiation of the hypodermis. Jones D; Candido E P. (Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, V6T 1Z3, Canada. ) Developmental biology, (2000 Oct 1) 226 (1) 152-65. Journal code: 0372762. ISSN: 0012-1606. Pub. country: United States. Language: English.
- AB This work has identified the enzymes involved in the activation and conjugation of the ubiquitin-like protein NED-8 in *Caenorhabditis elegans*. A *C. elegans* conjugating enzyme, UBC-12, is highly specific in its ability to utilize NED-8 as a substrate. Immunostaining shows that NED-8 is conjugated in vivo to a major target protein with a **conjugate** size of 90 kDa. While the amount of this **conjugate** is developmentally regulated with reduced levels in the larval stages, the mRNA encoding *C. elegans* UBC-12 is constitutively produced throughout development, as is NED-8 itself. The importance of the NED-8 conjugating system in *C. elegans* was determined by RNA interference (RNAi) assays using double-stranded RNA encoding NED-8, UBC-12, or the NED-8 activating enzyme component ULA-1. The progeny of both *ned-8* and *ubc-12* RNAi-treated hermaphrodites either arrested during embryonic development or underwent abnormal postembryonic development. The effect on postembryonic development was pleiotropic, the most frequent gross abnormality being vulval eversion during the L4 stage. Individuals with an everted vulva either burst at the L4 to adult molt or gave rise to adults incapable of egg laying. Additionally, both *ned-8* and *ubc-12* RNAi induced a striking abnormality in the alae, structures produced by the lateral hypodermal seam cells in the adult nematode. Affected alae were patchy and frequently diverged around a central space. Vulval defects were also produced by RNAi directed at *C. elegans* *ula-1*. This is the first demonstration of a requirement for NED-8 conjugation in metazoan development.  
 Copyright 2000 Academic Press.



2000441054. PubMed ID: 10839317. Acute acetaminophen toxicity in transgenic mice with elevated hepatic glutathione. Rzucidlo S J; Bounous D I; **Jones D P**; Brackett B G. (Department of Physiology and Pharmacology, College of Veterinary Medicine, University of Georgia, Athens 30602, USA. ) Veterinary and human toxicology, (2000 Jun) 42 (3) 146-50. Journal code: 7704194. ISSN: 0145-6296. Pub. country: United States. Language: English.

AB Previous studies demonstrated that elevation of hepatic glutathione (GSH) concentrations protect against acetaminophen (APAP) hepatotoxicity in mice. Employing transgenic mice overexpressing glutathione synthetase, this study was conducted to determine if sustained elevation of hepatic GSH concentrations could ameliorate or prevent APAP toxicity. International Cancer Research transgenic mouse males and matched (ie same strain, sex, and age) control nontransgenic mice were pretreated ip with GSH synthetase substrate gamma-glutamylcysteinyl ethyl ester (gamma-GCE) or with saline. After a 16-h fast, mice received a single dose of 500 mg APAP/kg bw in saline ip and were sacrificed 4 h later. Other mice similarly pretreated were killed without APAP challenge. The elevated GSH concentrations in transgenic mice livers did not lessen APAP hepatotoxicity. Instead higher degrees of hepatotoxicity and nephrotoxicity were observed in transgenic mice than in controls as indicated by higher serum alanine aminotransferase activity and more severe histopathological lesions in transgenic mice livers and kidneys. Pretreatment with gamma-GCE did not affect either initial or post-APAP treatment tissue GSH concentrations or observed degrees of toxicity. Detection of a higher level of serum APAP in transgenic mice and the histopathological lesions found in transgenic mice kidneys together with no observable nephrotoxicity in control mice indicated early kidney damage in transgenic mice. Our findings suggest that high levels of GSH-APAP **conjugates** resulting from increased GSH concentrations in the livers of transgenic mice caused rapid kidney damage. Compromised excretory ability may have caused retention of APAP, which, in effect, elicited higher hepatotoxicity than that observed in nontransgenic mice.

L19 ANSWER 44 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN 2000:467679 Document No.: PREV200000467679. Tolerance activity and pharmacokinetics of multivalent beta2GPI domain one **conjugates** in an immunized animal model. Branks, Michael J. [Reprint author]; Davis, Todd H. [Reprint author]; Smith, Eric M.; Ramirez, David S. [Reprint author]; Campbell, Mary-Ann [Reprint author]; **Jones, David S.** [Reprint author]; Cockerill, Keith A. [Reprint author]. La Jolla Pharmaceutical Company, 6455 Nancy Ridge Drive, San Diego, CA, USA. Journal of Autoimmunity, (Sept., 2000) Vol. 15, No. 2, pp. A5. print. Meeting Info.: 9th International Symposium on Antiphospholipid Antibodies. Tours, France. September 12-16, 2000. ISSN: 0896-8411. Language: English.

L19 ANSWER 45 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN 1999:795964 Document No. 132:49017 Therapeutic and diagnostic domain 1 of human  $\beta$ 2GPI polypeptides and methods of using same. Marquis, David M.; Iverson, Gilbert M.; Victoria, Edward J.; **Jones, David S.**; Linnik, Matthew D. (La Jolla Pharmaceutical Company, USA). PCT Int. Appl. WO 9964595 A1 19991216, 159 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US13194 19990609. PRIORITY: US 1998-88656 19980609; US 1998-103088 19981005; US 1999-328199 19990608.

AB Provided are domain 1 of  $\beta$ 2GPI polypeptides, polynucleotides encoding them, mimetics of these polypeptides, and methods using domain 1 of  $\beta$ 2GPI polypeptides and mimetics. Domain 1 of  $\beta$ 2GPI has been



shown to bind to anti-cardiolipin ( $\beta$ 2GPI-dependent anti-phospholipid) antibodies, which are associated with several pathologies, such as thrombosis and fetal loss. The domain 1 of  $\beta$ 2GPI polypeptides may be used to detect  $\beta$ 2GPI-dependent anti-phospholipid antibodies in a sample. Further provided are methods of inducing tolerance using these domain 1 of  $\beta$ 2GPI polypeptides. Synthesis of valency platform compds. and conjugation of the compds. with domain 1 were also demonstrated.

L19 ANSWER 46 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

2000:465651 Document No. 133:118957 Recombinant anti-bladder cancer immunotoxin and method of preparation. Huang, Hua; Huang, Haowen; Li, Zhihua; Yu, Lizhang; Lin, Qing; Zhang, Mingsheng (Heredity Inst., Chinese Academy of Sciences, Peop. Rep. China). Faming Zhuanli Shenqing Gongkai Shuomingshu CN 1229799 A 19990929, 30 pp. (Chinese). CODEN: CNXXEV. APPLICATION: CN 1999-103371 19990318.

AB Provided is an immunotoxin exhibiting anti-bladder cancer activity. The immunotoxin is a recombinant anti-bladder cancer antigen antibody conjugated with toxin protein. The recombinant antibody is selected from entire antibody mol., Fab, single domain antibody, and single chain antibody (scFv); and the toxin protein is selected from ricin, diphtheria toxin, and Pseudomonas exotoxin (PE) such as PE38. The anti-bladder cancer immunotoxin is prepared by mol. cloning with expression plasmid (vector) pAHM or pTMF in Escherichia coli as host cell.

L19 ANSWER 47 OF 161 MEDLINE on STN DUPLICATE 18

1999366857. PubMed ID: 10440245. Effect of dietary inducer dimethylfumarate on glutathione in cultured human retinal pigment epithelial cells. Nelson K C; Carlson J L; Newman M L; Sternberg P Jr; Jones D P; Kavanagh T J; Diaz D; Cai J; Wu M. (Department of Biochemistry, School of Medicine, Emory University, Atlanta, Georgia 30322, USA. ) Investigative ophthalmology & visual science, (1999 Aug) 40 (9) 1927-35. Journal code: 7703701. ISSN: 0146-0404. Pub. country: United States. Language: English.

AB PURPOSE: To determine the effect of dimethylfumarate (DMF), an inducer of glutathione (GSH)-dependent detoxification, on intracellular GSH levels in cultured human retinal pigment epithelium (hrPE) cells, its mechanism of action, and its effect on hrPE cells subjected to oxidative injury. METHODS: Established hrPE cell lines were treated with DMF and assayed by high-pressure liquid chromatography for intracellular and extracellular GSH levels. Quantification of gamma-glutamylcysteine synthetase (GLCL) was determined through northern and western blot analyses, and activity was measured. Effects of pretreatment with DMF on GSH redox status of hrPE cells was determined. Sensitivity of hrPE cells to oxidative stress was determined using tert-butylhydroperoxide as the oxidative agent. RESULTS: Dimethylfumarate caused a transient decrease followed by a significant increase in intracellular GSH. Glutathione increased maximally at 24 hours with 100 to 200 microM DMF. The initial decrease could be accounted for by the formation of a DMF-GSH conjugate. Dimethylfumarate treatment increased the steady state mRNA expression of the regulatory subunit of GLCL, but no increase was seen for the catalytic subunit. However, protein levels were increased for both, and the catalytic activity of GLCL was also increased. Whereas the initial decrease in GSH made hrPE cells more susceptible to oxidative damage, pretreatment with DMF under conditions that increased intracellular GSH protected hrPE cells against oxidative damage. CONCLUSIONS: These results suggest a means by which the antioxidant capability of hrPE may be augmented without direct antioxidant supplementation. Specifically, a dietary compound that conjugates with GSH can induce GSH synthesis, increase GSH concentration, and improve protection by GSH-dependent detoxification pathways in hrPE. However, the early depletion of GSH before stimulated synthesis necessitates caution in prevention strategies using dietary inducers.

L19 ANSWER 48 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 19

1999:866607 The Genuine Article (R) Number: 252ZU. Surface-enhanced Raman spectra studies on a novel dipyridophenazine complexes of ruthenium(II) and it's effect on DNA. **Yu L T (Reprint)**; Hu J M; Shen J K; He Z K; Wang X H. WUHAN UNIV, DEPT ANAL MEASUREMENT SCI, WUHAN 430072, PEOPLES R CHINA (Reprint); WUHAN UNIV, DEPT CHEM, WUHAN 430072, PEOPLES R CHINA. SPECTROSCOPY AND SPECTRAL ANALYSIS (OCT 1999) Vol. 19, No. 5, pp. 670-673. Publisher: BEIJING UNIV PRESS. HAIDIAN-QU, BEIJING 100871, PEOPLES R CHINA. ISSN: 1000-0593. Pub. country: PEOPLES R CHINA. Language: Chinese.

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB SERS is better method at analysing the samples which are prone to emit fluoescence or photodecomposition than other methods. Raman scattering of a novel complexes of Ruthenium( II ) :Ru(bpy)(2)dppz and it's effects on DNA were studied with surface-enhanced Raman spectra(SERS). We find that when this complex binds to DNA,only the ligand dppz intercalate into the double helix of DNA, and form a larger **conjugate** system, affect the metal-to-ligand charge transfer(MLCT),produce strong photoluminescence. All these cause shifting of some Raman peaks of the complex and changer of the relative intensity of some other peaks. And on the charge absorbed spectra, after the addition of DNA.,the compex' absorbed peaks of Ru(bpy)(2)dppz solvent shift to long wavelength, this is also one of the character of the intercalation.

L19 ANSWER 49 OF 161 MEDLINE on STN DUPLICATE 20  
1999278166. PubMed ID: 10346881. Multivalent thioether-peptide **conjugates**: B cell tolerance of an anti-peptide immune response. **Jones D S; Coutts S M**; Gamino C A; Iverson G M; Linnik M D; Randow M E; Ton-Nu H T; Victoria E J. (La Jolla Pharmaceutical Company, 6455 Nancy Ridge Drive, San Diego, California 92121, USA.. dave.jones@ljpc.com) . Bioconjugate chemistry, (1999 May-Jun) 10 (3) 480-8. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.

AB Antibodies which bind beta2-glycoprotein I (beta2GPI) are associated with antiphospholipid syndrome. Synthetic peptide mimotopes have been discovered which compete with beta2GPI for binding to selected anti-beta2GPI. A thiol-containing linker was attached to the N-terminus of two cyclic thioether peptide mimotopes, peptides 1a and 1b. The resulting peptides, with linker attached, were reacted with two different haloacetylated platforms to prepare four tetravalent peptide-platform **conjugates** to be tested as B cell toleragens. The linker-containing peptides were reacted with maleimide-derivatized keyhole limpet hemocyanin (KLH) to provide peptide-KLH **conjugates**. Peptides 1a and 1b were also modified by acylation with 3-(4'-hydroxyphenyl)propionic acid N-hydroxysuccinimidyl ester. The resulting hydroxyphenyl peptides were radioiodinated and used to measure anti-peptide antibody levels. The KLH **conjugates** were used to immunize mice to generate an anti-peptide immune response. The immunized mice were treated with the **conjugates** or saline solution and boosted with the appropriate peptide-KLH **conjugate**. Three of the four **conjugates** suppressed the formation of anti-peptide antibody. The stabilities of the **conjugates** in mouse serum were measured, and the relative stabilities did not correlate with ability to suppress antibody formation.

L19 ANSWER 50 OF 161 MEDLINE on STN DUPLICATE 21  
2000044039. PubMed ID: 10579438. Salivary antibodies following parenteral immunization of infants with a meningococcal serogroup A and C conjugated vaccine. Borrow R; Fox A J; Cartwright K; Begg N T; **Jones D M**. (Meningococcal Reference Unit, Manchester Public Health Laboratory, Withington Hospital, West Didsbury, UK. ) Epidemiology and infection, (1999 Oct) 123 (2) 201-8. Journal code: 8703737. ISSN: 0950-2688. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Bacterial and viral salivary antibody testing is proving sensitive and specific, useful for epidemiological studies, and is simple and non-invasive. Salivary serogroup C polysaccharide-specific (SC PS-S) IgA

and IgG were determined as a proportion of total salivary IgA and IgG in a group of UK infants who were recipients of a conjugated A/C meningococcal PS vaccine. Geometric mean concentrations (GMCs) of salivary SC PS-S IgG per mg of total IgG (microg/mg) were 0.1 pre-vaccination, rising to 8.2 post first, 16.1 post second and 29.3 post third dose of vaccine. For IgA, the corresponding GMCs in ng/mg were 0.1, 82.8, 69.6 and 91.2. Significant correlations ( $P < 0.0001$ ) were found between serum Ig and salivary IgG SC PS-S antibody for pre-vaccine and 1 month post each dose of vaccine suggesting that SC PS-S IgG in saliva was largely derived from serum. Of the five infants whose sera were analysed for isotype-specific responses, only traces of IgM and IgA were measurable suggesting that the SC PS-S IgA was locally produced. These findings suggests that the widespread use of meningococcal **conjugate** vaccines is likely to reduce nasopharyngeal carriage and may thereby induce herd immunity in the vaccinated population.

L19 ANSWER 51 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1999:774654 Document No. 132:290536 Biodistribution and radioimmunoimaging of 99Tcm-YDPC (monoclonal antibody) in nude mice bearing prostate carcinoma. Zhang, Chunli; Dou, Liqiang; **Yu, Lizhang**; Nie, Tao (The First Hospital, Beijing Medical University, Beijing, 100034, Peop. Rep. China). Tongweisu, 12(3), 151-154 (Chinese) 1999. CODEN: TONGEM. ISSN: 1000-7512. Publisher: Yuanzineng Chubanshe.

AB 99Tcm-YDPC was prepared by Schwartz direct reduction method. The in vitro immunoreactive fraction and associate constant were measured by Lindmo method and Scatchard method resp. 14.4 MBq 99Tcm-YDPC was injected into nude mice bearing human PC-3M prostate cancer, and measured after 24 h. The results showed that the labeling yield of 99Tcm-YDPC was up to 41-65%, the immunoreactive fraction and associate constant of 99Tcm-YDPC to prostate cancer cell line PC-3M were 58.1% and  $7.71 \times 10^9$  L/mol resp. The radioactivity ratio of tumor to non-tumor tissues (T/NT) was  $>2.00$  except that of tumor over blood and lung after 22 h pose injection, which was higher than that of colon tumor group. The imaging results showed that radioactivity concentration existed on tumor site in nude mice bearing prostate cancer, but

no

radioactivity concentration on colon tumor. 99Tcm-YDPC had excellent immunoreactivity and tumor locating property, and the radiolabeled YDPC may be useful for the diagnosis or therapy of prostate cancer.

L19 ANSWER 52 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 22

1999:155261 Document No.: PREV199900155261. Selective B cell non-responsiveness in the gut of the rainbow trout (*Oncorhynchus mykiss*). **Jones, Darren R.**; Hannan, Carolyn M.; Russell-Jones, Gregory J.; Raison, Robert L. [Reprint author]. Immunobiol. Unit. Aquaculture CRC, Univ. Technol., PO Box 123 Broadway, Sydney, NSW 2007, Australia. Aquaculture, (March 1, 1999) Vol. 172, No. 1-2, pp. 29-39. print. CODEN: AQCLAL. ISSN: 0044-8486. Language: English.

AB In order to assess the potential for the development of economically viable and effective oral vaccines we have examined the humoral immune response resulting from the anal administration of a hapten-carrier **conjugate** in the posterior intestine of the rainbow trout, *Oncorhynchus mykiss*. Fish were administered FITC-conjugated KLH either intraperitoneally (ip) or perianally (pa). Fish immunised pa with FITC-KLH developed significant anti-FITC antibodies in the serum by week 8. However, anti-KLH antibodies were not detected in these fish indicating an apparent selective B cell non-responsiveness to KLH in the gut. Fish immunised ip with FITC-KLH developed strong antibody titres to both hapten and carrier indicating that the failure to respond to this antigen via the mucosal route is not reflected in systemic non-responsiveness to KLH. The failure of FITC-KLH to elicit an anti-KLH response in the gut was not a consequence of epitope dominance on the part of the hapten as fish receiving KLH alone via the gut were also non-responsive to this normally immunogenic protein. Finally, fish previously immunised pa with FITC-KLH or unconjugated KLH and found to be non-responsive to KLH developed

anti-KLH antibodies when immunised ip with KLH 21 and 11 weeks, respectively, after first receiving pa antigen. Thus the failure to mount an anti-KLH response in these fish is not a result of the induction of systemic tolerance to the carrier. The results suggest that while the intestinal lymphoid tissue of the trout contains KLH reactive T cells, as reflected in the ability to mount a strong anti-hapten response, there is a lack of responsive KLH-specific B cells in this tissue. This may reflect either a restriction in the repertoire of gut-associated B cells compared to those in the peripheral tissues, or the induction of an anergic state in the KLH-specific population.

L19 ANSWER 53 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1999:27732 Document No. 130:86184 Vaccines containing Bordetella pertussis antigen. Farrar, Graham Henry; Jones, David Hugh (Microbiological Research Authority, UK). PCT Int. Appl. WO 9858668 A2 19981230, 30 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-GB1819 19980622. PRIORITY: GB 1997-13156 19970620.

AB A vaccinating **conjugate** comprises an antigen conjugated to a carrier selected from Bordetella pertussis fimbria, pertussis toxin, pertussis toxoid, and pertussis 69kD protein. The **conjugate** may also comprise a second antigen, different from the first. An oral vaccinating composition comprises Bordetella pertussis fimbria or fimbria-antigen **conjugate**.

L19 ANSWER 54 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1998:81695 Document No. 128:141135 Synthesis of Novel Poly( $\epsilon$ -caprolactone)s Functionalized with a Thioester End-Group via a Living Ring Opening Polymerization and Their Application in Chemoselective Ligation with Compounds Containing a Cysteine Terminal. Ni, Qiang; Yu, Luping (Department of Chemistry, University of Chicago, Chicago, IL, 60637, USA). Journal of the American Chemical Society, 120(7), 1645-1646 (English) 1998. CODEN: JACSAT. ISSN: 0002-7863. Publisher: American Chemical Society.

AB A facile method for the introduction of a thioester end-group in the ring-opening polymerization of  $\sigma$ -caprolactone ( $\epsilon$ -CL) using dimethylaluminum benzylthiolate as an initiator has been developed. The living character shown in the polymerization process has enabled us to synthesize

PCL-b-PLA block copolymer in a controlled way. More importantly, the chemoselective ligation approach has been demonstrated to be applicable to thioester functionalized PCL. This may provide a new approach for the design and synthesis of novel PCL **conjugates** such as PCL-peptide **conjugates**.

L19 ANSWER 55 OF 161 MEDLINE on STN DUPLICATE 23

1999302577. PubMed ID: 10374347. Targeted diagnosis and treatment of superficial bladder cancer with monoclonal antibody BDI-1. Yu L; Gu F; Zhang C; Xie S; Guo Y. (First Hospital, Beijing Medical University, China. ) Chinese medical journal, (1998 May) 111 (5) 404-7. Journal code: 7513795. ISSN: 0366-6999. Pub. country: China. Language: English.

AB OBJECTIVE: To explore the application of monoclonal antibody (McAb) to targeted treatment of bladder carcinoma through a series of in vitro and in vivo studies carried out in animal model and patients with bladder carcinoma. METHODS: Monoclonal antibody BDI-1 against bladder carcinoma was prepared by the lymphocyte hybridoma technique. McAb was conjugated with  $^{99m}\text{Tc}$  by direct reduction method. Momodin (MD) was covalently linked to McAb by SPDP method. Radioimmunoimaging of nude mice xenografts and patients with bladder carcinoma were performed with BDI-1- $^{99m}\text{Tc}$  **conjugates**. An immunotoxin (BDI-1-MD) was inducted via a catheter into the bladder. Targeted treatment with BDI-1-MD was carried out in 18 patients. RESULTS: This study showed the specificity of McAb, and clear imaging of nude mice bearing xenografts. Distribution analysis of  $^{99m}\text{Tc}$ -BDI-1 in nude mice showed the highest value of T/NT in bladder

tumor. Targeted diagnosis and treatment for patients by intravesical administration are very safe and effective. CONCLUSION: The bladder cancer seems an ideal model for diagnostic and therapeutic approaches using regional administration of McAb **conjugates** via a catheter direct into the bladder.

L19 ANSWER 56 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1998:648288 Document No. 129:343786 Synthesis of thioester end-functionalized poly(.vepsiln.-caprolactone) and its application in chemoselective ligation. Ni, Qiang; **Yu, Luping** (Department of Chemistry and The James Franck Institute, The University of Chicago, Chicago, IL, 60637, USA). ACS Symposium Series, 709(Tailored Polymeric Materials for Controlled Delivery Systems), 92-104 (English) 1998. CODEN: ACSMC8. ISSN: 0097-6156. Publisher: American Chemical Society.

AB In order to synthesize novel poly(.vepsiln.-caprolactone) (PCL) **conjugates**, thioester functionalized PCL has been synthesized by using dimethylaluminum benzylthiolate as an initiator. The living character and quant. introduction of thioester end in this ring opening polymerization (ROP) process have been confirmed by GPC and 1H NMR characterization. Furthermore, the applicability of chemoselective ligation to the thioester end has been demonstrated with compds. containing a cysteine terminal.

L19 ANSWER 57 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

2002:62199 Document No.: PREV200200062199. Chemically-defined non-polymeric valency platform molecules and **conjugates** thereof. **Coutts, S. M.** [Inventor]; **Jones, D. S.** [Inventor]; **Livingston, D. A.** [Inventor]; **Yu, L.** [Inventor]. Rancho Santa Fe, Calif., USA. ASSIGNEE: LA JOLLA PHARMACEUTICAL COMPANY. Patent Info.: US 5606047 Feb. 25, 1997. Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 25, 1997) Vol. 1195, No. 4, pp. 2594-2595. print. CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

L19 ANSWER 58 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1998:1383 Document No. 128:61804 aPL immunoreactive peptides and their **conjugates** for treatment of aPL antibody-mediated pathologies. Victoria, Edward Jess; Marquis, David Matthew; **Jones, David S.**; **Yu, Lin** (Lajolla Pharmaceutical Company, USA; Victoria, Edward Jess; Marquis, David Matthew; Jones, David S.; Yu, Lin). PCT Int. Appl. WO 9746251 A1 19971211, 155 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US10075 19970606. PRIORITY: US 1996-660092 19960606; US 1996-760508 19961205.

AB APL analogs that bind specifically to B cells to which an aPL epitope binds are disclosed. Optimized analogs lacking T cell epitope(s) are useful as **conjugates** for treating aPL antibody-mediated diseases. **Conjugates** comprising aPL analogs and nonimmunogenic valency platform mols. are provided as are novel nonimmunogenic valency platform mols. and linkers. Methods of preparing and identifying said analogs, methods of treatment using said analogs, methods and compns. for preparing **conjugates** of said analogs and diagnostic immunoassays for aPL antibodies are disclosed.

L19 ANSWER 59 OF 161 MEDLINE on STN

DUPLICATE 24

97362286. PubMed ID: 9211943. The smallest membrane anchoring subunit (QPs3) of bovine heart mitochondrial succinate-ubiquinone reductase. Cloning, sequencing, topology, and Q-binding domain. Shenoy S K; **Yu L**; Yu C A. (Department of Biochemistry & Molecular Biology, Oklahoma State University, Stillwater, OK 74078, USA.) Journal of biological

chemistry, (1997 Jul 11) 272 (28) 17867-72. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB The cDNA encoding the smallest membrane-anchoring subunit (QPs3) of bovine heart mitochondrial succinate-ubiquinone reductase was cloned and sequenced. This cDNA is 1330 base pairs long with an open reading frame of 474 base pairs that encodes the 103 amino acid residues of mature QPs3 and a 55-amino acid residue presequence. The cDNA insert has an 820-base pair long 3'-untranslated region, including a poly(A) tail. The molecular mass of QPs3, deduced from the nucleotide sequence, is 10,989 Da. QPs3 is a very hydrophobic protein; the hydropathy plot of the amino acid sequence reveals three transmembrane helices. Previous photoaffinity labeling studies of succinate-ubiquinone reductase, using 3-azido-2-methyl-5-methoxy[3H]-6-decyl-1,4-benzoquinone ([3H]azido-Q), identified QPs3 as one of the putative Q-binding proteins in this reductase. An azido-Q-linked peptide with a retention time of 66 min is obtained by high performance liquid chromatography of the chymotrypsin digest of carboxymethylated and succinylated [3H]azido-Q-labeled QPs3 purified from labeled succinate-ubiquinone reductase by a procedure involving phenyl-Sepharose 4B column chromatography, preparative SDS-polyacrylamide gel electrophoresis, and acetone precipitation. The amino acid sequence of this peptide is NH<sub>2</sub>-L-N-P-C-S-A-M-D-Y-COOH, corresponding to residues 29-37. The structure of QPs3 in the inner mitochondrial membrane is proposed based on the hydropathy profile of the amino acid sequence, on the predicted tendencies to form alpha-helices and beta-sheets, and on immunobinding of Fab' fragment horseradish peroxidase **conjugates** prepared from antibodies against two synthetic peptides, corresponding to the NH<sub>2</sub> terminus region and the loop connecting helices 2 and 3 of QPs3, in mitoplasts and submitochondrial particles. The ubiquinone-binding domain in the proposed model of QPs3 is probably located at the end of transmembrane helix 1 toward the C-side of the mitochondrial inner membrane.

L19 ANSWER 60 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 25

97:756646 The Genuine Article (R) Number: YA003. Experimental investigation by stimulated Brillouin scattering of incomplete phase conjugation. **Jones D C (Reprint)**; Ridley K D. DEF RES AGCY, ST ANDREWS RD, MALVERN WR14 3PS, WORCS, ENGLAND (Reprint). JOURNAL OF THE OPTICAL SOCIETY OF AMERICA B-OPTICAL PHYSICS (OCT 1997) Vol. 14, No. 10, pp. 2657-2663. Publisher: OPTICAL SOC AMER. 2010 MASSACHUSETTS AVE NW, WASHINGTON, DC 20036. ISSN: 0740-3224. Pub. country: ENGLAND. Language: English. \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB We use stimulated Brillouin scattering to investigate phase conjugation of a laser beam aberrated by one or more phase screens when the aberrated beam is incompletely sampled by the phase-**conjugate** mirror. Good agreement is found between our experimental results and previous theoretical work. We find that the fraction of the reflected beam that is phase **conjugate** after the double pass is proportional to the fraction of the original beam sampled by the phase-**conjugate** mirror. We also show that it is possible to increase the resolution of a phase-**conjugate** mirror by inserting an aberrator.

L19 ANSWER 61 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1997:579489 Document No. 127:221065 Synthesis of novel functionalized poly-epsilon-caprolactone: a facile method for the introduction of thioester end-group. Ni, Qiang; Zhu, William; **Yu, Luping** (Department of Chemistry and The James Frank Institute, The University of Chicago, Chicago, IL, 60637, USA). Polymer Preprints (American Chemical Society, Division of Polymer Chemistry), 38(2), 584-585 (English) 1997. CODEN: ACPPAY. ISSN: 0032-3934. Publisher: American Chemical Society, Division of Polymer Chemistry.

AB A facile method for introduction of a thioester group via ring opening polymerization of epsilon-caprolactone using a catalyst system based on trimethylaluminum and benzylthiol as initiator was developed. The living character of the polymerization process allowed synthesis of polycaprolactone-

polylactide [PCL-b-PLA] block copolymers in a controlled manner. The selective bond formation can also be used to obtain thioester-functionalized polycaprolactones. This method can be used for design and synthesis of novel PCL **conjugates** such as PCL-peptides.

L19 ANSWER 62 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1997:489400 Synthesis of novel functionalized poly-ε-caprolactone: A facile method for the introduction of thioester end-group.. Ni, Qiang; Zhu, William; **Yu, Luping** (Department Chemistry, University Chicago, Chicago, IL, 60637, USA). Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11, POLY-263. American Chemical Society: Washington, D. C. (English) 1997. CODEN: 64RNAO.

AB In order to synthesize novel poly-ε-caprolactone (PCL) **conjugates**, thioester functionalized PCL has been synthesized by using dimethylaluminum benzylthiolate as an initiator. The living character and quant. introduction of thioester end in this ring opening polymerization (ROP) process have been confirmed by GPC and <sup>1</sup>H NMR characterization. Furthermore, the applicability of chemoselective ligation to the thioester end has been demonstrated with small model compound

L19 ANSWER 63 OF 161 MEDLINE on STN

DUPLICATE 26

97275826. PubMed ID: 9129587. Non-culture diagnosis and serogroup determination of meningococcal B and C infection by a sialyltransferase (siaD) PCR ELISA. Borrow R; Claus H; Guiver M; Smart L; **Jones D M**; Kaczmarek E B; Frosch M; Fox A J. (Manchester Public Health Laboratory, Withington Hospital, UK. ) Epidemiology and infection, (1997 Apr) 118 (2) 111-7. Journal code: 8703737. ISSN: 0950-2688. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Rapid, non-culture, serogroup determination of meningococcal infection is important in contact management where vaccination may be possible. The impending availability of polysaccharide-protein **conjugate** vaccines for serogroup C disease requires maximal case ascertainment, with serogroup determination, at a time when the number of culture confirmed meningococcal infections is decreasing. A polymerase chain reaction assay (PCR), based on a restriction fragment length polymorphism (RFLP) in the meningococcal serogroup B and C sialyltransferase (siaD) gene, was developed to combine the non-culture diagnosis of meningococcal infection from CSF, whole blood and serum with serogroup (B and C) identification. The PCR assay was adapted to an ELISA format incorporating hybridization with serogroup-specific B and C oligonucleotide probes. Specificity for CSFs was 100% and sensitivities were respectively 81, 63 and 30% for CSFs, whole blood and sera. The serogroup-specific PCR ELISA is a significant addition to currently available tests for non-culture diagnosis of meningococcal infection and outbreak investigation.

L19 ANSWER 64 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

97:666277 The Genuine Article (R) Number: XQ859. Synthesis of a trisaccharide gal(alpha 1-3)gal(beta 1-4)glc, an antigen of anti-gal antibody, and its PEG-linked mannosyl **conjugates**. **Yu L B (Reprint)**; Wang J Q; Xie W H; Fang J W; Wang P G. UNIV MIAMI, DEPT CHEM, CORAL GABLES, FL 33124. ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY (7 SEP 1997) Vol. 214, Part 2, pp. 107-ORGN. Publisher: AMER CHEMICAL SOC. 1155 16TH ST, NW, WASHINGTON, DC 20036. ISSN: 0065-7727. Pub. country: USA. Language: English.

L19 ANSWER 65 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1997:488510 Synthesis of a trisaccharide Gal(alpha 1-3)Gal(beta 1-4)Glc, an antigen of anti-gal antibody, and its PEG-linked mannosyl **conjugates**. **Yu, Libing**; Wang, Jianqiang; Xie, Wenhua; Fang, Jianwen; Wang, Peng George (Department Chemistry, University Miami, Coral Gables, FL, 33124, USA). Book of Abstracts, 214th ACS National Meeting, Las Vegas, NV, September 7-11, ORGN-107. American Chemical Society: Washington, D. C. (English) 1997. CODEN: 64RNAO.

AB The synthesis of the title trisaccharide will be presented from

peracetylated lactose and galactose. The key alpha linkage between two galactose is constructed through thioglycoside chemical with methylthio galactoside as donor. 1-Azido group in glucose unit was especially designed to enable to connect any other interesting moieties. PEG-linked Mannosyl **conjugate** is synthesized since mannose can specifically bind to cell surfaces of some bacteria and the terminal trisaccharide may result in strong immuno reactions to lead to killing of the cells. The research is aimed at designing and synthesizing novel therapeutical agents based on immuno interactions between anti-gal antibody and its antigens.

L19 ANSWER 66 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 27

97:416400 The Genuine Article (R) Number: XA785. Characterisation of liquid brillouin media at 532 nm. **Jones D C (Reprint)**. DRA, LASER & PHOTON DEPT, ST ANDREWS RD, MALVERN, WORCS, ENGLAND (Reprint). JOURNAL OF NONLINEAR OPTICAL PHYSICS & MATERIALS (MAR 1997) Vol. 6, No. 1, pp. 69-79. Publisher: WORLD SCIENTIFIC PUBL CO PTE LTD. JOURNAL DEPT PO BOX 128 FARRER ROAD, SINGAPORE 9128, SINGAPORE. ISSN: 0218-1991. Pub. country: ENGLAND. Language: English.

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB A number of transparent liquids have been evaluated for use in stimulated Brillouin scattering at 532 nm. Measurements were made of frequency shift, SBS threshold, reflectivity and optical breakdown properties. It was found that the alkanes, and in particular n-pentane, performed well and measurements were made of Brillouin gain coefficient and phonon lifetimes. It is suggested that these liquids are promising candidates for use in self-pumped phase **conjugate** mirrors, high gain Brillouin amplifiers and four-wave mixing mirrors.

L19 ANSWER 67 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN 1997:428934 Document No.: PREV199799728137. Synthesis of a trisaccharide Gal(alpha 1-3)Gal(beta 1-4)Glc, an antigen of anti-Gal antibody, and its PEG-linked mannosyl **conjugates**. **Yu, Libing**; Wang, Jianqiang; Xie, Wenhua; Fang, Jianwen; Wang, Peng George. Dep. Chem., Univ. Miami, PO Box 249118, Coral Gables, FL 33124, USA. Abstracts of Papers American Chemical Society, (1997) Vol. 214, No. 1-2, pp. ORGN 107. Meeting Info.: 214th American Chemical Society National Meeting. Las Vegas, Nevada, USA. September 7-11, 1997. CODEN: ACSRAL. ISSN: 0065-7727. Language: English.

L19 ANSWER 68 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 28

2002:48444 Document No.: PREV200200048444. Chemically-defined non-polymeric valency platform molecules and **conjugates** thereof. **Coutts, S. M.** [Inventor]; **Jones, D. S.** [Inventor]; **Livingston, D. A.** [Inventor]; **Yu, L.** [Inventor]. Rancho Santa Fe, Calif., USA. ASSIGNEE: LA JOLLA PHARMACEUTICAL COMPANY. Patent Info.: US 5552391 Sept. 3, 1996. Official Gazette of the United States Patent and Trademark Office Patents, (Sept. 3, 1996) Vol. 1190, No. 1, pp. 437-438. print. CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

L19 ANSWER 69 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1997:141010 Document No. 126:143310 Immunoreactive peptides, **conjugates** and methods for treatment of antiphospholipid (aPL) antibody-mediated pathologies. Victoria, Edward Jess; Marquis, David Matthew; **Jones, David S.**; **Yu, Lin** (La Jolla Pharmaceutical Company, USA). PCT Int. Appl. WO 9640197 A1 19961219, 118 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US9976 19960606. PRIORITY: US 1995-482651 19950607.

AB APL analogs that bind specifically to B cells to which an aPL epitope



binds are disclosed. Optimized analogs lacking T cell epitope(s) are useful as **conjugates** for treating aPL antibody-mediated diseases. Methods of preparing and identifying said analogs, methods of treatment using said analogs, methods and compns. for preparing **conjugates** of said analogs and diagnostic immunoassays for aPL antibodies are disclosed.

L19 ANSWER 70 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1996:685465 Document No. 125:326409 The gClq receptor, HIV-1 gp120 region binding thereto, and related peptides and targeting antibodies. Fung, Michael S. C.; Sun, Bill N. C.; Sun, Cecily R. Y.; Kim, Young Woo; **Yu, Liming** (Tanox Biosystems, Inc., USA). PCT Int. Appl. WO 9630400 A1 19961003, 69 pp. DESIGNATED STATES: W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SE, SI, SK, TJ, TT, UA, UZ, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US3905 19960322. PRIORITY: US 1995-410360 19950324.

AB Disclosed are immunogens and peptides based on the binding site of gClq-R for HIV-1 gp120, and immunogens and peptide based on the binding site of HIV-1 gp 120 for gClq-R. Both of the sequence of the gClq-R binding site for gp120 and the sequence of HIV-1 gp120 binding site for gClq-R are presented. Also disclosed are antibodies and binding mols. to all such immunogens and peptides, and inducing the endogenous production of such antibodies. GClq-R-encoded cDNA was prepared and expressed in Escherichia coli, and monoclonal antibodies against gClq-R were raised and binding to HIV-1 IIIB gp120 and HIV-1 neutralization were characterized.

L19 ANSWER 71 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

96:488955 The Genuine Article (R) Number: UT784. STEREOSELECTIVE EFFICIENT SYNTHESIS OF BICYCLO[2.2.1]HEPTANE DERIVATIVES VIA INTRAMOLECULAR MICHAEL REACTIONS OF VINYL SULFONES. COLLINS M A (Reprint); **JONES D N**. WYETH AYERST RES, 145 KING OF PRUSSIA RD, RADNOR, PA, 19087 (Reprint); UNIV SHEFFIELD, DEPT CHEM, SHEFFIELD S3 7HF, S YORKSHIRE, ENGLAND. TETRAHEDRON (24 JUN 1996) Vol. 52, No. 26, pp. 8795-8806. ISSN: 0040-4020. Pub. country: USA; ENGLAND. Language: ENGLISH.

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Efficient synthesis of 6-endo-methyl substituted bicyclo[2.2.1]heptane derivatives formed via completely diastereoselective intramolecular Michael addition reactions of vinyl sulfones, derived from allyl sulfones and cyclopentenones, are described. Copyright (C) 1996 Published by Elsevier Science Ltd

L19 ANSWER 72 OF 161 MEDLINE on STN

DUPLICATE 29

97094147. PubMed ID: 8940235. **Conjugate** meningococcal serogroup A and C vaccine: reactogenicity and immunogenicity in United Kingdom infants. Fairley C K; Begg N; Borrow R; Fox A J; **Jones D M**; Cartwright K. (Public Health Laboratory Service, Communicable Disease Surveillance Centre, London, United Kingdom. ) Journal of infectious diseases, (1996 Dec) 174 (6) 1360-3. Journal code: 0413675. ISSN: 0022-1899. Pub. country: United States. Language: English.

AB The reactogenicity and immunogenicity of a serogroup A and C meningococcal polysaccharide-CRM197 **conjugate** vaccine was evaluated in 58 infants who received three doses at 2, 3, and 4 months of age. The **conjugate** vaccine produced few systemic side effects, and local reactions were significantly less common than those produced by the routine vaccinations. The prevaccination geometric mean titers (GMTs) of A and C polysaccharide antibodies were, respectively, 2.8 and 0.6 microg/mL, rising to 21.5 and 38.5 microg/mL by 1 month after the third dose (age 5 months) and falling to 3.1 and 2.2 microg/mL by 14 months of age. Prevaccination serum bactericidal titers against 2 serogroup C meningococci strains were <1/4 in 49 of 52 infants, rising to a GMT of 1/3082 at 1 month after the third dose and falling by age 14 months to a GMT of 1/10. Thus, this meningococcal **conjugate** vaccine proved to be safe and immunogenic, inducing high levels of anti-C polysaccharide

antibodies that were bactericidal in young infants.

- L19 ANSWER 73 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
1996:542538 Document No. 125:237772 The synovial membrane, liver, and tongue: target organs for a ricin A-chain immunotoxin (ZD0490). Westwood, F. Russell; Jones, David V.; Aldridge, Andrew (Safety Medicines Department, ZENECA Pharmaceuticals, Macclesfield, Cheshire, SK10 4TG, UK). Toxicologic Pathology, 24(4), 477-483 (English) 1996. CODEN: TOPADD. ISSN: 0192-6233. Publisher: Toxicologic Pathology.
- AB ZD0490 is an immunotoxin consisting of a mouse monoclonal antibody conjugated to recombinant ricin A-chain (rRAC). It was developed at Zeneca Pharmaceuticals as a treatment for certain antigen-bearing tumors. During safety evaluation studies in rats, a number of reversible inflammatory changes were seen. The synovial membranes of articular joints showed a marked degeneration and necrosis with an associated inflammation. When of mild severity only the synovial membrane was involved, but when more severe many adjacent tissues including the surface of the articular cartilage were affected. Some nonspecific skeletal muscle toxicity occurred. However, tongues from the i.v. (tail) dosed rats consistently showed inflammation specifically located in the ventral subepithelial area with myocyte degeneration and necrosis. Also, hepatic peliosis primarily located in the subcapsular areas was induced. Studies with rRAC alone indicated that ricin A-chain (RAC) is the component responsible for these findings. It is suggested that cells of a macrophage type with the ability to specifically bind RAC may at least in part determine the location and nature of the changes seen.
- L19 ANSWER 74 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE  
30  
96:205233 The Genuine Article (R) Number: TZ375. TIME RESPONSE OF BRILLOUIN-INDUCED 4-WAVE-MIXING WITH SHORT SIGNAL PULSE - APPLICATION TO TIME-GATED IMAGING. JONES D C (Reprint); RIDLEY K D. DRA MALVERN, ST ANDREWS RD, GREAT MALVERN, WORCS, ENGLAND (Reprint). OPTICS COMMUNICATIONS (15 JAN 1996) Vol. 123, No. 1-3, pp. 403-411. ISSN: 0030-4018. Pub. country: ENGLAND. Language: ENGLISH.  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*
- AB We investigate the time response of a phase **conjugate** mirror based on Brillouin-induced four-wave mixing, with a signal pulse that is shorter than the pump pulse. We show that, with suitable tailoring of the temporal profiles of signal and pump pulses, Brillouin-induced four-wave mixing can be used for time-gated phase **conjugate** imaging with a depth resolution on the order of 1 metre.
- L19 ANSWER 75 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
1996:416164 Metal complex - containing conjugated polymers with large photorefractivity.. Peng, Z. H.; Gharavi, A. R.; Yu, L. (Dept. Chem., Univ. Chicago, Chicago, IL, 60637, USA). Book of Abstracts, 212th ACS National Meeting, Orlando, FL, August 25-29, POLY-397. American Chemical Society: Washington, D. C. (English) 1996. CODEN: 63BFAF.
- AB A new **conjugate** polymer containing an ionic transition metal complex and a NLO chromophore was synthesized by utilizing the Heck coupling reaction. The ruthenium complex was applied to enhance the photocharge generation efficiency through its MLCT transition while the **conjugate** backbone was designed to enhance the charge transporting process. Phys. measurements clearly demonstrated that our designed polymer indeed has an enhanced photocond. and large photorefractive effect.
- L19 ANSWER 76 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE  
31  
96:205209 The Genuine Article (R) Number: TZ375. A STIMULATED BRILLOUIN-SCATTERING PHASE-**CONJUGATE** MIRROR HAVING A PEAK-POWER THRESHOLD LESS-THAN-100 W. JONES D C (Reprint); MANGIR M S; ROCKWELL D A. HUGHES RES LABS, OPT PHYS LAB, 3011 MALIBU CANYON RD, MALIBU, CA, 90265 (Reprint). OPTICS COMMUNICATIONS (15 JAN 1996) Vol. 123,

No. 1-3, pp. 175-181. ISSN: 0030-4018. Pub. country: USA. Language: ENGLISH.

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB We have demonstrated stimulated Brillouin scattering phase conjugation in a hollow glass lightguide filled with CS<sub>2</sub>. Threshold peak powers were as low as 70 W, and the reflectivity and conjugation fidelity reached 50% and 80%, respectively. The SBS threshold and reflectivity were unchanged with average input powers up to 20 W.

L19 ANSWER 77 OF 161 MEDLINE on STN DUPLICATE 32  
96400488. PubMed ID: 8806864. Compartmentation of glutathione: implications for the study of toxicity and disease. Smith C V; Jones D P; Guenther T M; Lash L H; Lauterburg B H. (Department of Pediatrics, Baylor College of Medicine, Houston 77030, USA. ) Toxicology and applied pharmacology, (1996 Sep) 140 (1) 1-12. Ref: 82. Journal code: 0416575. ISSN: 0041-008X. Pub. country: United States. Language: English.

AB The fact that glutathione (GSH) plays many roles in biological protective mechanisms and critical physiological functions has been recognized for decades. **Conjugates**, disulfides, and other glutathione-derived products also have been studied as biomarkers of the chemical natures or specific identities of key metabolites of toxic agents and such studies have been crucial in the delineation of the nature of the interactions of proximal toxicants with target biomolecules. Despite the extensive evidence implicating the depletion and/or oxidation of glutathione in a wide variety of human and experimental toxicities, critical examination of such studies frequently reveals that injury is not simply related to glutathione status. GSH is compartmentalized at several levels and this compartmentation appears to exert considerable influence on the relationships between glutathione depletion or oxidation and the onset of injury. Although compartmentation is usually viewed from the perspective of different intracellular pools, the significance of extracellular glutathione in functionally important pools is gaining recognition. As the factors affecting the interactions of intracellular pools with extracellular pools are delineated, studies in humans can be designed and interpreted with greater precision and utility.

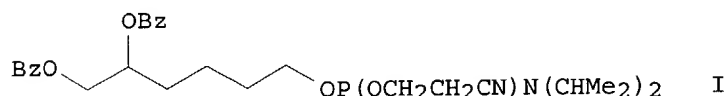
L19 ANSWER 78 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
1996:170767 Document No. 124:194291 Use of  $\beta$ -GalNac(1-4) $\beta$ Gal **conjugates** to treat Candida infection. Yu, Lei; Lee, Kok Kheong; Sheth, Hasmukh B.; Irvin, Randall T.; Hodges, Robert S. (S.P.I. Synthetic Peptides Inc., Can.). PCT Int. Appl. WO 9535111 A2 19951228, 63 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-IB514 19950616. PRIORITY: US 1994-261487 19940617.

AB A method of treating Candida albicans infection is disclosed. In one embodiment, for treatment of oral or vaginal infection, the treatment is by topical application of a composition of **conjugates** that are each composed of a carrier structure and multiple  $\beta$ GalNac(1-4) $\beta$ Gal moieties attached to the structure. In another embodiment, for treatment of systemic infection, the treatment is by parenteral administration of a humanized form of a mouse monoclonal antibody produced by mouse hybridoma cell line Fm16 or cell line PK99H.  $\beta$ GalNac(1-4) $\beta$ Gal Me ester inhibited binding of Candida fimbriae to epithelial cells. Production and characterization of mouse monoclonal anti-fimbrial antibodies are described, as are purification and characterization of Candida fimbrial protein.

L19 ANSWER 79 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
1995:532240 Document No. 122:291459 Phosphoramidite intermediates for providing functional groups on the 5' end of oligonucleotides. Jones, David S.; Hachmann, John P.; Conrad, Michael J.; Coutts, Stephen; Livingston, Douglas A. (La Jolla Pharmaceutical Company, USA). U.S. US 5391785 A 19950221, 14 pp. Cont.-in-part of U.S. Ser. No. 731,055, abandoned. (English). CODEN:

USXXAM. APPLICATION: US 1992-915589 19920715. PRIORITY: US 1990-466138 19900116; US 1990-494118 19900313; US 1991-731055 19910715.

GI



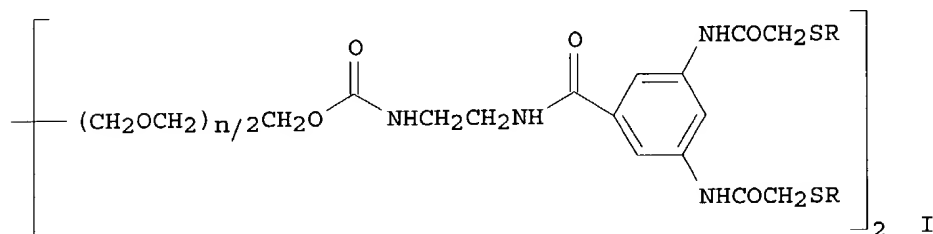
AB Phosphoramidites of the formula  $ROP(NR_1R_2)OGZ$  where R is a base-labile protecting group,  $R_1$  and  $R_2$  are individually alkyl of 1 to 6 carbon atoms, cycloalkyl of 3 to 8 carbon atoms, or aryl of 6 to 20 carbon atoms or are joined together to form with the nitrogen atom a cyclic structure of 4-7 carbon atoms and 0 to 1 annular chalcogen atoms of atomic number 8 to 16, G is

a

hydrocarbylene group of 1 to 20 carbon atoms and Z is a hydroxy-protected vicinal diol group bound to G by one of the vicinal diol carbon atoms or a disulfide group and bound to G by one of the sulfur atoms of the disulfide group, with the proviso that G is of at least 4 carbon atoms when Z is said disulfide group are used in conventional automated oligonucleotide synthesis to introduce a functional aldehyde or thiol group on the 5' end of the oligonucleotide to thereby provide a reactive site on the oligonucleotide that may be used to **conjugate** the oligonucleotide to mols. that contain a free amino group or an electrophilic center reactive with a thiol group. Thus, e.g., reaction of 5,6-bis(O-benzoyl)-1,5,6-hexanetriol (preparation given) with O-cyanoethyl N,N,N',N'-tetraisopropylphosphorodiamidite in presence of diisopropylammonium tetrazolide afforded phosphoramidite I (93%) which was sequentially coupled to a control glass supported oligonucleotide, oxidized, and then conjugated with D-glutamic acid-D-lysine copolymer and with keyhole limpet hemocyanin.

L19 ANSWER 80 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 1995:892826 Document No. 124:290272 Preparation of chemically-defined non-polymeric valency platform molecules and **conjugates** thereof.. **Coutts, Stephen; Jones, David S.; Livingston, Douglas Alan; Yu, Lin** (La Jolla Pharmaceutical Co., Can.). Eur. Pat. Appl. EP 642798 A2 19950315, 76 pp.  
 DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1993-309720 19931203. PRIORITY: US 1993-118055 19930908; US 1993-142598 19931022; US 1993-152506 19931115; EP 1993-309288 19931122.

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AB **Conjugates** comprising biol. or chemical mols., including polynucleotide duplexes of at least 20 base pairs that have significant binding activity for human lupus anti-dsDNA autoantibodies, reacted with valency platforms  $G_1(T_1)_n$ ,  $G_2[L_2J_2Z_2(pT_2)]_m$  [ $G_1$ ,  $G_2$  = null, (branched) chain containing 1-2000 atoms selected from C, N, O, Si, P, S;  $T_1$ ,  $T_2$  = NHR,

CONHNHR, NHNHR, CO<sub>2</sub>H, CO<sub>2</sub>R1, COX, SO<sub>2</sub>X, SH, OH, etc.; R = H, alkyl, cycloalkyl, aralkyl; R1 = N-succinimidyl, p-nitrophenyl, pentafluorophenyl, etc.; X = halo, other leaving group; L2 = null, O, NR, S; J2 = null, CO, CS; Z2 = radical containing 1-200 atoms selected from C, H, N, O, Si, P, S, and containing attachment sites for functional groups; n, m = 1-32; p = 1-8; with provisos], were prepared. Thus, title **conjugate** (I; R = H-Trp-Ile-Lys-Arg-Lys-Arg-Gln-Gln-Lys-Cys-Gly-OH, bound through a cysteine S atom; n = approx. 74) (preparation given) at 1000 µg/mouse in mice primed and boosted with the parent protein melittin gave an 86.8% reduction in peptide specific plaque forming cells.

L19 ANSWER 81 OF 161 MEDLINE on STN DUPLICATE 33  
 95302433. PubMed ID: 7783145. Immunospecific reduction of antioligonucleotide antibody-forming cells with a tetrakis-oligonucleotide **conjugate** (LJP 394), a therapeutic candidate for the treatment of lupus nephritis. **Jones D S**; Barstad P A; Feild M J; Hachmann J P; Hayag M S; Hill K W; Iverson G M; **Livingston D A**; Palanki M S; Tibbetts A R; +. (La Jolla Pharmaceutical Company, San Diego, California 92121, USA. ) Journal of medicinal chemistry, (1995 Jun 9) 38 (12) 2138-44. Journal code: 9716531. ISSN: 0022-2623. Pub. country: United States. Language: English.

AB A discrete tetravalent **conjugate**, 7a (LJP 394), consisting of four oligonucleotides attached to a common carrier or platform was prepared. Single-stranded oligonucleotide 20-mers consisting of alternating deoxycytidine-deoxyadenosine nucleotides, (CA)<sub>10</sub>, were attached to a tetrabromoacetylated platform by displacement with sulfhydryl-terminated linkers. The tetrabromoacetylated platform 3a was synthesized in three steps using triethylene glycol bis-(chloroformate). The single-stranded **conjugate** was characterized by polyacrylamide gel electrophoresis, DNA sequencing, phosphate analysis, carbon and nitrogen combustion analysis, and correlation of stoichiometry to conversion in the conjugation process. HPLC and capillary electrophoretic methods were developed to evaluate purity. The tetrakis, single-stranded **conjugate** was annealed with a stoichiometric amount of a complementary single-stranded oligonucleotide 20-mer consisting of alternating thymidine-deoxyguanosine nucleotides, (TG)<sub>10</sub>. The double-stranded **conjugate** LJP 394 was characterized by melt temperature and hyperchromicity, phosphate analysis, and carbon and nitrogen combustion analysis. LJP 394 inhibits binding of DNA to anti-double-stranded oligonucleotide antibodies and reduces anti-oligonucleotide-specific plaque (antibody)-forming cells in an immunized mouse model by a proposed mechanism involving cross-linking B cell surface immunoglobins.

L19 ANSWER 82 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
 95:269714 The Genuine Article (R) Number: QP711. RESPONSE OF A BRILLOUIN AMPLIFIER AND 4-WAVE-MIXING MIRROR TO A SPECTRALLY BROADENED SIGNAL BEAM. **JONES D C (Reprint)**; SCOTT A M; STEWART I. DEF RES AGCY, ST ANDREWS RD, MALVERN WR14 3PS, WORCS, ENGLAND (Reprint). OPTICS LETTERS (01 APR 1995) Vol. 20, No. 7, pp. 692-694. ISSN: 0146-9592. Pub. country: ENGLAND. Language: ENGLISH.

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB We show that, when the input signal to a Brillouin amplifier and a phase-**conjugate** mirror is spectrally broadened, the Brillouin interaction can still efficiently amplify and **conjugate** the input.

L19 ANSWER 83 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 1994:261341 Document No. 120:261341 **Conjugates** of biologically stable polyfunctional molecules and polynucleotides for treating systemic lupus erythematosus (SLE). Conrad, Michael J.; **Coutts, Stephen** (La Jolla Pharmaceutical Co., USA). U.S. US 5276013 A 19940104, 21 pp. Cont.-in-part of U.S. 5,162,515. (English). CODEN: USXXAM. APPLICATION: US 1992-914869 19920715. PRIORITY: US 1990-466138 19900116; US 1990-494118 19900313.

AB Chemical defined **conjugates** are disclosed which consist of biol. stable valency platform mols., e.g. copolymers of D-glutamic acid and D-lysine or PEG, and polynucleotide duplexes of  $\geq 20$  base pairs that have significant binding activity for human lupus anti-dsDNA autoantibodies. The duplexes are preferably homogeneous in length structure and are bound to the valency platform mol. via reaction between a functional group located at or proximate a terminus of each duplex and functional groups on the valency platform mol. The **conjugates** are tolerogens for human SLE. Thus a **conjugate** of D-glutamic acid-D-lysine copolymer with (AC)30:(TG)30 was prepared and tested as a tolerogen in a murine model for human SLE.

L19 ANSWER 84 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
94:659596 The Genuine Article (R) Number: PL145. HETERODIENE CYCLOADDITIONS - PREPARATION AND TRANSFORMATIONS OF SOME SUBSTITUTED PYRANO[4,3-B][1]BENZOPYRANS. **COUTTS S J**; WALLACE T W (Reprint). UNIV SALFORD, DEPT CHEM & APPL CHEM, SALFORD M5 4WT, LANCS, ENGLAND (Reprint); UNIV SALFORD, DEPT CHEM & APPL CHEM, SALFORD M5 4WT, LANCS, ENGLAND. TETRAHEDRON (03 OCT 1994) Vol. 50, No. 40, pp. 11755-11780. ISSN: 0040-4020. Pub. country: ENGLAND. Language: ENGLISH.  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Heterodiene cycloadditions of 4-oxo-4H-1-benzopyrans with formyl, acetyl, or carboxyl substituents at C-3 to 1-alkoxy- or 1,1-dialkoxyalkenes produce 3-alkoxy- or 3,3-dialkoxy-4,4a-dihydropyrano[4,3-b][1]benzopyran-10-ones which are capable of a variety of selective transformations, including acid-induced epimerisation and/or retro-cycloaddition, reduction, hydrolysis and alcoholysis, in some cases under very mild conditions.

L19 ANSWER 85 OF 161 MEDLINE on STN DUPLICATE 34  
94274300. PubMed ID: 8005674. Fimbria-mediated adherence of *Candida albicans* to glycosphingolipid receptors on human buccal epithelial cells. **Yu L**; Lee K K; Sheth H B; Lane-Bell P; Srivastava G; Hindsgaul O; Paranchych W; Hodges R S; Irvin R T. (Department of Medical Microbiology and Infectious Diseases, University of Alberta, Edmonton, Canada.) Infection and immunity, (1994 Jul) 62 (7) 2843-8. Journal code: 0246127. ISSN: 0019-9567. Pub. country: United States. Language: English.

AB *Candida albicans* is an opportunist fungal pathogen that has the ability to adhere to host cell surface receptors via a number of adhesins. Yu et al. (L. Yu, K. K. Lee, K. Ens, P. C. Doig, M. R. Carpenter, W. Staddon, R. S. Hodges, W. Paranchych, and R. T. Irvin, Infect. Immun. 62:2834-2842, 1994) described the purification and initial characterization of a fimbrial adhesin from *C. albicans*. In this paper, we show that *C. albicans* fimbriae also bind to asialo-GM1 [gangliotetraosylceramide: beta Gal(1-3)beta GalNAc(1-4) beta Gal(1-4)beta Glc(1-1)Cer] immobilized on microtiter plates in a saturable and concentration-dependent manner. *C. albicans* fimbrial binding to exfoliated human buccal epithelial cells (BECs) was inhibited by asialo-GM1 in in vitro binding assays. The fimbriae interact with the glycosphingolipid receptors via the carbohydrate portion of the receptors, since fimbriae were observed to bind to synthetic beta GalNAc(1-4)beta Gal-protein **conjugates** and the disaccharide was able to inhibit binding of fimbriae to BECs in in vitro binding assays. We conclude from these results that the *C. albicans* yeast form expresses a fimbrial adhesin that binds to glycosphingolipids displayed on the surface of human BECs.

L19 ANSWER 86 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 35  
94:740319 The Genuine Article (R) Number: PT162. AN 8.2 J-PHASE-**CONJUGATE** SOLID-STATE LASER COHERENTLY COMBINING 8 PARALLEL AMPLIFIERS. SUMIDA D S (Reprint); **JONES D C**; ROCKWELL D A. HUGHES RES LABS, OPT PHYS LAB, DEPT ADV LASER SOURCES, MALIBU, CA, 90265 (Reprint). IEEE JOURNAL OF QUANTUM ELECTRONICS (NOV 1994) Vol. 30, No. 11, pp. 2617-2627. ISSN: 0018-9197. Pub. country: USA. Language: ENGLISH.  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB We describe a phase-conjugate master oscillator-power amplifier configuration in which as many as eight parallel flashlamp-pumped Cr:Nd:GSGG amplifiers and four parallel CD\* A frequency doubling crystals were coherently combined. Operating at a pulse repetition frequency of 1.25 Hz, we demonstrated an output energy of 8.2 J at 1  $\mu$ m and 4.4 J at 530 nm for a 54% frequency-doubling efficiency. This effort represents the highest reported output energy achieved using coherent coupling via phase conjugation. In subsequent experiments at a pulse repetition frequency of 5 Hz, we produced approximately 22 W of 1.06  $\mu$ m average power with a beam quality that was approximately 2.5 times diffraction-limited. The observed far-field intensity profile indicates that we achieved effective and consistent compensation of optical-path length differences among the multiple parallel amplifiers and frequency-doubling crystals.

L19 ANSWER 87 OF 161 MEDLINE on STN DUPLICATE 36  
95029911. PubMed ID: 7943347. Glutathione transport by type II cells in perfused rat lung. Bai C; Brown L A; Jones D P. (Department of Biochemistry, Emory University School of Medicine, Atlanta, Georgia 30322. ) American journal of physiology, (1994 Oct) 267 (4 Pt 1) L447-55. Journal code: 0370511. ISSN: 0002-9513. Pub. country: United States. Language: English.

AB Glutathione (GSH) is an antioxidant that protects the lung against oxidative-injury. Most cells rely on synthesis of GSH to maintain intracellular supply and only a few cell types take up intact GSH. Although isolated type II cells from rat have a Na(+)-dependent uptake system that transports GSH into the cells against a concentration gradient, it is not known whether this occurs from the vasculature in the intact lung or whether other cell types in the lung also transport GSH. Based on the knowledge that gamma-glutamyl analogues of GSH are also transported by the Na(+)-GSH transporter, a method was developed and used to study the cell specificity of GSH uptake in perfused lung. A stable, fluorescent GSH S-conjugate (GSH-I14) was synthesized and separated from the original dye as analyzed by high-performance liquid chromatography. Studies with isolated alveolar type II cells showed that uptake of GSH-I14 was Na+ dependent and inhibited by GSH. In addition, uptake of GSH by the type II cells was inhibited by GSH-I14. After perfusion of the isolated rat lung with GSH-I14, the conjugate accumulated primarily in the alveolar type II cell as observed by fluorescence microscopy. This was confirmed by isolation of type II cells and measurement of GSH-I14 content. Thus these results show that specificity of GSH transport can be studied with the fluorescent derivative, GSH-I14, and that in the isolated perfused lung type II cells can transport and concentrate GSH-I14 from the perfusate. Quantitative fluorescence microscopy will be required to further determine relative transport activities by other cell types.

L19 ANSWER 88 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
95:31414 The Genuine Article (R) Number: PW555. GLUTATHIONE TRANSPORT BY TYPE-II CELLS IN PERFUSED RAT LUNG. BAI C L; BROWN L A S; JONES D P (Reprint). EMORY UNIV, SCH MED, DEPT BIOCHEM, ATLANTA, GA, 30322 (Reprint); EMORY UNIV, SCH MED, DEPT BIOCHEM, ATLANTA, GA, 30322; EMORY UNIV, SCH MED, DEPT PEDIAT, ATLANTA, GA, 30322. AMERICAN JOURNAL OF PHYSIOLOGY-LUNG CELLULAR AND MOLECULAR PHYSIOLOGY (OCT 1994) Vol. 11, No. 4, pp. L447-L455. ISSN: 1040-0605. Pub. country: USA. Language: ENGLISH. \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Glutathione (GSH) is an antioxidant that protects the lung against oxidative injury. Most cells rely on synthesis of GSH to maintain intracellular supply and only a few cell types take up intact GSH. Although isolated type II cells from rat have a Na+-dependent uptake system that transports GSH into the cells against a concentration gradient, it is not known whether this occurs from the vasculature in the intact lung or whether other cell types in the lung also transport GSH. Based on the knowledge that gamma-glutamyl analogues of GSH are also transported by the Na+-GSH transporter, a method was developed and used to

study the cell specificity of GSH uptake in perfused lung. A stable, fluorescent GSH S-**conjugate** (GSH-I14) was synthesized and separated from the original dye as analyzed by high-performance liquid chromatography. Studies with isolated alveolar type II cells showed that uptake of GSH-I14 was Na<sup>+</sup> dependent and inhibited by GSH. In addition, uptake of GSH by the type II cells was inhibited by GSH-I14. After perfusion of the isolated rat lung with GSH-I14, the **conjugate** accumulated primarily in the alveolar type II cell as observed by fluorescence microscopy. This was confirmed by isolation of type II cells and measurement of GSH-I14 content. Thus these results show that specificity of GSH transport can be studied with the fluorescent derivative, GSH-I14, and that in the isolated perfused lung type II cells can transport and concentrate GSH-I14 from the perfusate. Quantitative fluorescence microscopy will be required to further determine relative transport activities by other cell types.

- L19 ANSWER 89 OF 161 MEDLINE on STN DUPLICATE 37  
 95151807. PubMed ID: 7849067. **Conjugates** of double-stranded oligonucleotides with poly(ethylene glycol) and keyhole limpet hemocyanin: a model for treating systemic lupus erythematosus. **Jones D S**; Hachmann J P; Osgood S A; Hayag M S; Barstad P A; Iverson G M; **Coutts S M.** (La Jolla Pharmaceutical Company, San Diego, California 92121. ) Bioconjugate chemistry, (1994 Sep-Oct) 5 (5) 390-9. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.
- AB Two types of oligonucleotides were synthesized with linker groups attached at the 5'-end. Both were repeating dimers of deoxyribocytidine and deoxyriboadenosine. A 20-mer was prepared with a thiol-containing linker, masked as a disulfide, and a 50-mer was prepared with a vicinal diol-containing linker. A tetraiodoacetylated poly(ethylene glycol) (PEG) derivative was synthesized and reacted with the thiol-containing 20-mer to provide an oligonucleotide PEG **conjugate** of precisely four oligonucleotides on each PEG carrier. The vicinal diol on the 50-mer was oxidized to an aldehyde and conjugated to keyhole limpet hemocyanin (KLH) to provide an oligonucleotide-KLH **conjugate** by reductive alkylation. The **conjugates** were annealed with complementary (TG)<sub>n</sub> strands. While the double-stranded oligonucleotide-KLH **conjugate** is an immunogen, eliciting the synthesis of antibodies against oligonucleotides, the PEG **conjugate** has the biological property of specifically suppressing (tolerizing) B cells which make antibodies against the immunizing oligonucleotide.

- L19 ANSWER 90 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
 94:137312 The Genuine Article (R) Number: MY954. LJP-249 - A NEW OLIGONUCLEOTIDE **CONJUGATE** FOR SUPPRESSION OF ANTI-DOUBLE STRANDED DNA ANTIBODIES. **JONES D S (Reprint)**; HACHMANN J P; OSGOOD S A; **COUTTS S M.** LA JOLLA PHARMACEUT, SAN DIEGO, CA, 92121. ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY (13 MAR 1994) Vol. 207, Part 1, pp. 113-BIOT. ISSN: 0065-7727. Pub. country: USA. Language: ENGLISH.

- L19 ANSWER 91 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
 1994:192936 Document No.: PREV199497205936. LJP-249: A new oligonucleotide **conjugate** for suppression of anti-double stranded DNA antibodies. **Jones, David S.**; Hachmann, John P.; Osgood, Stephen A.; **Coutts, Stephen M.** La Jolla Pharmaceutical Company, 6455 Nancy Ridge Dr., San Diego, CA 92121, USA. Abstracts of Papers American Chemical Society, (1994) Vol. 207, No. 1-2, pp. BIOT 113. Meeting Info.: 207th National Meeting of the American Chemical Society. San Diego, California, USA. March 13-17, 1994. CODEN: ACSRAL. ISSN: 0065-7727. Language: English.

- L19 ANSWER 92 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE  
 38  
 93:689813 The Genuine Article (R) Number: MG738. ASYMMETRIC-SYNTHESIS OF LIGNANS OF THE DIBENZYL BUTANEDIOL AND TETRAHYDRODIBENZOCYCLOOCTENE SERIES.



PELTER A (Reprint); WARD R S; JONES D M; MADDOCKS P. SWANSEA UNIV, DEPT CHEM, SINGLETON PK, SWANSEA SA2 8PP, WALES (Reprint); WELLCOME FDN LTD, DARTFORD DA1 5AH, KENT, ENGLAND. JOURNAL OF THE CHEMICAL SOCIETY-PERKIN TRANSACTIONS 1 (07 NOV 1993) No. 21, pp. 2631-2637. ISSN: 0300-922X. Pub. country: WALES; ENGLAND. Language: ENGLISH.  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Enolate anions obtained by **conjugate** addition to (-)-5-(1-menthyloxy)furan-2(5H)-one are quenched with benzyl bromides or iodides to yield homochiral dibenzylbutyrolactones. Desulfurisation followed by lithium aluminium hydride reduction affords homochiral 2,3-dibenzylbutane-1,4-diols, including (-)-dimethylsecoisolariciresinol and (-)-dihydroclusin. Desulfurisation followed by reduction with NaBH<sub>4</sub>/KOH gives the homochiral 2,3-dibenzylbutyrolactones (-)-dimethylmatairesinol, (-)-kusunokinin and (-)-yatein, which undergo stereoselective oxidative coupling with DDQ in trifluoroacetic acid to give homochiral tetrahydrodibenzocyclooctene lignans belonging to the isostegane series.

L19 ANSWER 93 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 39

93:689812 The Genuine Article (R) Number: MG738. ASYMMETRIC-SYNTHESIS OF DIBENZYL BUTYROLACTONES AND ARYL TETRALIN LIGNAN LACTONES BY TANDEM **CONJUGATE** ADDITION TO A CHIRAL BUTENOLIDE. PELTER A (Reprint); WARD R S; JONES D M; MADDOCKS P. SWANSEA UNIV, DEPT CHEM, SINGLETON PK, SWANSEA SA2 8PP, WALES (Reprint); WELLCOME FDN LTD, DARTFORD DA1 5AH, KENT, ENGLAND. JOURNAL OF THE CHEMICAL SOCIETY-PERKIN TRANSACTIONS 1 (07 NOV 1993) No. 21, pp. 2621-2629. ISSN: 0300-922X. Pub. country: WALES; ENGLAND. Language: ENGLISH.  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Addition of sulfur-stabilised carbanions to (-)-5-(1-menthyloxy)furan-2(5H)-one followed by reaction with an aromatic aldehyde affords a short synthesis of enantiomerically pure dibenzylbutyrolactone derivatives. Desulfurisation with NaBH<sub>4</sub>/NiCl<sub>2</sub> proceeds in almost quantitative yield, and reduction with NaBH<sub>4</sub>/KOH gives the parent dibenzylbutyrolactones including (-)-6-epipodophyllotoxin. These undergo cyclisation with acid to give homochiral aryltetralins including (-)-deoxyisopodophyllotoxin in high yield.

L19 ANSWER 94 OF 161 MEDLINE on STN DUPLICATE 40  
93267584. PubMed ID: 8496911. 2'-substituted chalcone derivatives as inhibitors of interleukin-1 biosynthesis. Batt D G; Goodman R; Jones D G; Kerr J S; Mantegna L R; McAllister C; Newton R C; Nurnberg S; Welch P K; Covington M B. (Inflammatory Diseases Research, Du Pont Merck Pharmaceutical Co., Wilmington, Delaware 19880-0353. ) Journal of medicinal chemistry, (1993 May 14) 36 (10) 1434-42. Journal code: 9716531. ISSN: 0022-2623. Pub. country: United States. Language: English.

AB A series of 2'-substituted chalcone derivatives has been found to show potent inhibition of the production of IL-1 beta from human peripheral blood monocytes stimulated with lipopolysaccharide (LPS), with IC<sub>50</sub> values in the 0.2-5.0-microM range. Some members of the series have also shown inhibition of septic shock induced in mice by injection of LPS, although with low potency. Qualitative structure-activity relationships have shown that the enone is required for activity, which may be mediated by **conjugate** addition of a biological nucleophile to the chalcone. Electron-poor aromatic rings beta to the ketone give enhanced potency. Although electronic effects in the other ring (directly attached to the ketone) are minimal, this ring must possess an ortho substituent for good activity without cytotoxicity, suggesting a degree of selectivity which would not be expected for simple, nonspecific alkylating agents.

L19 ANSWER 95 OF 161 MEDLINE on STN DUPLICATE 41  
94144196. PubMed ID: 8310708. Metabolism and enantioselective pharmacokinetics of Casodex in man. McKillop D; Boyle G W; Cockshott I D; Jones D C; Phillips P J; Yates R A. (Safety of Medicines Department, ICI Pharmaceuticals, Alderley Park, Macclesfield, Cheshire,

UK. ) Xenobiotica; fate of foreign compounds in biological systems, (1993 Nov) 23 (11) 1241-53. Journal code: 1306665. ISSN: 0049-8254. Pub. country: ENGLAND: United Kingdom. Language: English.

- AB 1. Five healthy male volunteers received a single oral dose (50 mg; 42 microCi) of <sup>14</sup>C-Casodex, a racemic compound, which has its antiandrogen activity predominantly in R-Casodex, the (-)-enantiomer, with little activity in S-Casodex, the (+)-enantiomer. 2. Plasma concentrations of R-Casodex increased slowly in all subjects to reach a peak of 559-970 ng/ml between 15 and 48 h after dosing and, thereafter, declined monoexponentially with a mean half-life of 4.2 days. Plasma concentrations of S-Casodex rose rapidly to reach a peak of 32-66 ng/ml within the first 2-5 h, and then declined monoexponentially with a mean half-life of 19 h. Plasma concentrations of the racemate were in very good agreement with the sum of the enantiomer concentrations throughout the study and were very similar to concentrations of total radioactivity over the first 4 days. 3. About 80% of the radioactive dose was recovered in urine (35.8 +/- 1.7%; mean +/- SEM) and faeces (42.6 +/- 2.9%) during a total collection over 9 days; this incomplete recovery was consistent with the slow elimination of R-Casodex. 4. T.l.c. of urine extracts indicated extensive metabolism of Casodex to two polar metabolites identified as the glucuronide **conjugates** of Casodex and hydroxy-Casodex; almost no parent compound was observed. Virtually all of the Casodex glucuronide excreted in urine during the first 2 days was derived from S-Casodex, consistent with the relatively low plasma concentrations and rapid elimination of this enantiomer. 5. T.l.c. of faecal extracts showed the presence of both Casodex and hydroxy-Casodex; these may have been eliminated in bile as the glucuronide **conjugates**, with subsequent hydrolysis in the intestinal tract.

L19 ANSWER 96 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
93:157109 The Genuine Article (R) Number: KQ824. CURRENT AND FUTURE-TRENDS IMMUNIZATION AGAINST MENINGITIS. JONES D M (Reprint). WITHINGTON HOSP, MANCHESTER PUBL HLTH LAB, MANCHESTER M20 8LR, LANCS, ENGLAND (Reprint). JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY (FEB 1993) Vol. 31, Supp. B, pp. 93-99. ISSN: 0305-7453. Pub. country: ENGLAND. Language: ENGLISH.

L19 ANSWER 97 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
93:101701 The Genuine Article (R) Number: KM367. MENINGOCOCCAL VACCINES. JONES D M (Reprint). PUBL HLTH LAB, MANCHESTER M20 8LR, ENGLAND (Reprint). JOURNAL OF MEDICAL MICROBIOLOGY (FEB 1993) Vol. 38, No. 2, pp. 77-78. ISSN: 0022-2615. Pub. country: ENGLAND. Language: ENGLISH.

L19 ANSWER 98 OF 161 MEDLINE on STN DUPLICATE 42  
93192515. PubMed ID: 8448354. Selective depletion of mitochondrial glutathione concentrations by (R,S)-3-hydroxy-4-pentenoate potentiates oxidative cell death. Shan X; Jones D P; Hashmi M; Anders M W. (Department of Biochemistry, Emory University, Atlanta, Georgia 30322. ) Chemical research in toxicology, (1993 Jan-Feb) 6 (1) 75-81. Journal code: 8807448. ISSN: 0893-228X. Pub. country: United States. Language: English.

- AB The hepatocellular glutathione content is partitioned into a cytosolic pool, which accounts for about 85% of the cellular glutathione content, and a mitochondrial pool, which accounts for about 15% of the cellular glutathione content. Previous studies indicated that the mitochondrial glutathione pool may play a critical role in cytoprotection against xenobiotic-induced cell damage. Tests of the role of mitochondrial glutathione in cytoprotection have been hampered by the lack of agents that selectively deplete the mitochondrial glutathione pool. To test the hypothesis that mitochondrial glutathione plays a critical role in protecting against cytotoxic agents, we developed a method to deplete selectively mitochondrial glutathione concentrations. (R,S)-3-Hydroxy-4-pentenoate, an analog of (R)-3-hydroxybutanoate, caused a rapid and selective depletion of mitochondrial glutathione concentrations. Incubation of (R,S)-3-hydroxy-4-pentenoate with rat liver mitochondria or

with 3-hydroxybutyrate dehydrogenase in the presence of glutathione afforded a glutathione **conjugate** whose chromatographic properties were identical with synthetic S-(3-oxo-4-carboxybutyl)glutathione, indicating that (R,S)-3-hydroxy-4-pentenoate was oxidized to the Michael acceptor 3-oxo-4-pentenoate, which reacts with glutathione. Exposure of rat hepatocytes to (R,S)-3-hydroxy-4-pentenoate, which was not cytotoxic and did not induce mitochondrial dysfunction, potentiated the cytotoxicity of tert-butyl hydroperoxide. These results establish the critical role of mitochondrial glutathione in cytoprotection and demonstrate and (R,S)-3-hydroxy-4-pentenoate may find utility in exploring mitochondrial glutathione homeostasis.

L19 ANSWER 99 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1993:53162 Document No. 118:53162 Thyroid-derived chondrocyte-stimulating factor. Smith, Lane R.; **Jones, Deryk G.** (Leland Stanford Junior University, USA). PCT Int. Appl. WO 9214749 A1 19920903, 31 pp. DESIGNATED STATES: W: JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US993 19920205. PRIORITY: US 1991-654965 19910213.

AB Thyroid-derived chondrocyte-stimulating factor (I) is a high-mol.-weight complex (>500 kDa) of proteinaceous subunits which can be at least partially dissociated into active portions by 8 M urea. I stimulates articular chondrocyte and synovial fibroblast growth under serum-free conditions. I is useful for the culture of chondrocytes and fibroblasts in vitro as a serum substitute, for developing cartilage implants in vitro, and for in vivo use in cartilage and bone defect repair and degenerative joint diseases. I is stabilized in the presence of reducing agents for disulfide bonds. Antibodies to I and **conjugates** of I are claimed. Isolation of I from bovine thyroid tissue is described.

L19 ANSWER 100 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1992:549290 Document No. 117:149290 Antibodies to membrane-bound IgM and IgD for suppression or stimulation of B-cells. Chang, Tse Wen; **Yu, Liming** (Tanox Biosystems, Inc., USA). PCT Int. Appl. WO 9207574 A1 19920514, 39 pp. DESIGNATED STATES: W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1991-US7886 19911022. PRIORITY: US 1990-603898 19901025; US 1991-740754 19910805.

AB Antibodies and anti-idiotypic antibodies to the IgM- $\alpha$  and IgD- $\alpha$  glycoproteins are disclosed, as well as peptides inducing the antibodies. The antibodies can be used to target and suppress or deplete resting or activated B-cells. The antibodies may be conjugated to toxins or to viral or bacterial antigens. Cloning and expression of the mb-1 gene for IgM- $\alpha$  is described.

L19 ANSWER 101 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1992:209133 Document No. 116:209133 Method for preparing, isolating, and sequencing polynucleotides. **Jones, David Stephen Charnock;** Schofield, Julian Paul; Vaudin, Mark (Medical Research Council, UK). PCT Int. Appl. WO 9203575 A1 19920305, 21 pp. DESIGNATED STATES: W: JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1991-GB1379 19910814. PRIORITY: GB 1990-17788 19900814.

AB A variation of the Hultman method for sequencing of nucleic acids (Nuc. Acids Res. (1989)17: 4937) is described. A nucleic acid target containing a separating label is prepared and mixed with a support matrix containing a group which

binds the separating label. to purify the target nucleic for sequencing. All of the steps in this sequence, i.e. the preparation of the target, the immobilization, and at least part of the sequencing step are performed in the same vessel. The target may be prepared by PCR amplification directly in M13,  $\lambda$  phage, or bacterial cells. The separating label (e.g. biotin) may be incorporated into the primer, and the support matrix may be a magnetic bead covalently coupled to streptavidin or avidin. This

procedure is amenable to automated screening and sequencing strategies.

L19 ANSWER 102 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1992:212834 Document No. 116:212834 The immunoenhancing class II protein of the outer membrane of *Neisseria meningitidis*. Oliff, Allen I.; Liu, Margaret A.; Friedman, Arther; Tai, Joseph Y.; Donnelly, John J.; **Jones, Deborah D.**; Montgomery, Donna L.; Lowe, Robert S. (Merck and Co., Inc., USA). Eur. Pat. Appl. EP 467714 A1 19920122, 73 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1991-306618 19910719. PRIORITY: US 1990-555329 19900719; US 1990-555204 19900719; US 1990-555978 19900719; US 1991-639457 19910110; US 1991-715274 19910619.

AB The class II major immunoenhancing protein (MIEP) of *N. meningitidis* is purified from the outer membrane of *N. meningitidis* or is obtained through recombinant cloning and expression of DNA encoding MIEP and has immunol. carrier as well as immunol. enhancement and mitogenic properties. MIEP (extracted and purified from *N. meningitidis* B11 serotype 2 or recombinantly produced) was conjugated with maleimidopropionyl cyclic peptides (synthesis given). Monkeys inoculated with the **conjugates** developed antibodies specific for the peptides.

L19 ANSWER 103 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1992:661097 Document No. 117:261097 Frequency detuning in Brillouin induced four-wave mixing. Ridley, K. D.; Scott, A. M.; **Jones, D. C.** (Def. Res. Agency, Great Malvern/Worcestershire, WR14 3PS, UK). International Journal of Nonlinear Optical Physics, 1(3), 563-80 (English) 1992. CODEN: IJNOEQ. ISSN: 0218-1991.

AB The effect was studied of tuning of the signal frequency in Brillouin induced 4-wave mixing. A number of theor. predictions were verified, and in the unstable regime the frequency of the phase **conjugate** is independent of the signal frequency.

L19 ANSWER 104 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

92:519375 The Genuine Article (R) Number: JK610. BRILLOUIN-INDUCED 4-WAVE-MIXING USING BEAMS WITH GAUSSIAN TEMPORAL AND SPATIAL PROFILES. **JONES D C (Reprint)**; RIDLEY K D; SCOTT A M. RSRE MALVERN, DRA ELECTR DIV, ST ANDREWS RD, GREAT MALVERN, WORCS, ENGLAND (Reprint). OPTICS COMMUNICATIONS (01 SEP 1992) Vol. 92, No. 4-6, pp. 393-402. ISSN: 0030-4018. Pub. country: ENGLAND. Language: ENGLISH. \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Numerical solutions are obtained to the coupled acoustic and optical field equations for the case where the signal beam is anti-Stokes shifted relative to the pump beam. It is shown that when gaussian temporal pulse profiles are used, the theoretically predicted reflectivity and efficiency are greatly modified owing to the strong dependence of **conjugate** build up time on signal and pump beam intensity. The effect of varying pulse length, phonon lifetime, and signal-pump timing is studied. Finally the effect of gaussian spatial profiles is considered.

L19 ANSWER 105 OF 161 MEDLINE on STN

92263202. PubMed ID: 1374935. Growth cones and structural variation of synaptic end-bulbs in the cochlear nucleus of the adult cat brain. **Jones D R**; Hutson K A; Morest D K. (Department of Anatomy, University of Connecticut Health Center, Farmington 06030. ) Synapse (New York, N.Y.), (1992 Apr) 10 (4) 291-309. Journal code: 8806914. ISSN: 0887-4476. Pub. country: United States. Language: English.

AB To explore the potential for structural variation and new growth at the synapse, we studied the morphological patterns of the end-bulbs of cochlear nerve axons in adult cats by using rapid Golgi, reduced silver, and electron microscopic methods. Horseradish peroxidase labeling of these endings in the anterior division of the antroventral cochlear nucleus was produced by anterograde transport following injection into the cochlea. Three types of end-bulbs were distinguished, regardless of method: reticular, coalescent, and ringed forms, all synapsing on spherical bushy cells. The reticular variety corresponds to the

classically described end-bulb and constitutes the majority in all regions of the tonotopic map. The ringed end-bulb, described here for the first time, forms an excitatory synaptic cuff around the base of a bushy cell's main dendrite; these endings were localized to the region receiving cochlear input in the 1-6 kHz range, which is used in vocalization. The coalescent ending forms a small fraction of the end-bulb population throughout the region studied. The findings raise the possibility of functional differences between these synaptic types. Growth cones and retraction clubs were present on most, if not all, of the end-bulbs in every adult cat studied. A systematic survey of the end-bulb patterns revealed a continuous gradient of variation, in which each synaptic type forms a distinct mode. These findings lead us to hypothesize that the end-bulbs are in a continual state of structural and functional flux. These endings should prove useful for studies on the modifiable properties of central synapses.

L19 ANSWER 106 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

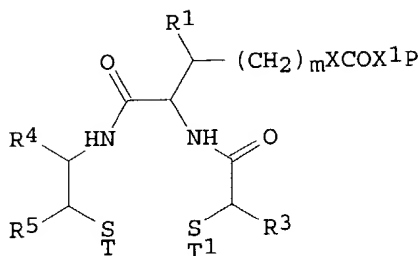
1992:167828 Document No. 116:167828 Polynucleotide amplification by sequential linear and exponential polymerase chain reaction. **Jones, David Stephen Charnock**; Rosenthal, Andre (Medical Research Council, UK). PCT Int. Appl. WO 9118114 A1 19911128, 73 pp. DESIGNATED STATES: W: JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1991-GB803 19910522. PRIORITY: GB 1990-11454 19900522.

AB A polynucleotide amplification method using linear PCR followed by exponential PCR is described. The target contains a (1st) region of known sequence and sticky ends. A cassette with complementary sticky ends is ligated to the target to produce a polynucleotide containing a 2nd known primer annealing region. The ligation product is denatured, a primer complementary to the 1st region and containing a separating label is added, and the primer is extended with a polymerase. The products of this linear amplification are denatured and isolated using an immobilized receptor for the separating label of the primer. The isolated polynucleotide is then subjected to exponential PCR amplification. This method can be used in genome walking and in extending cDNA sequences.

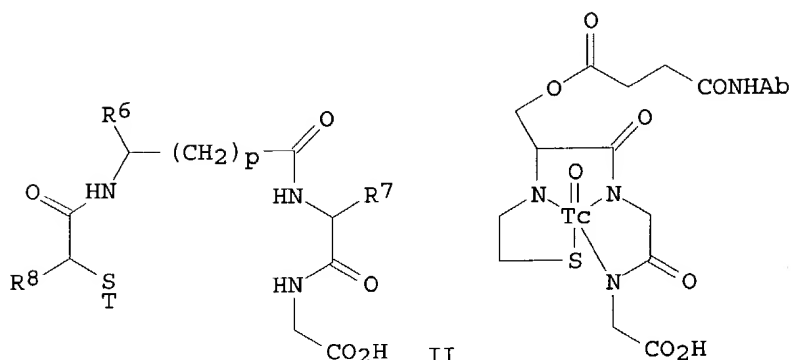
L19 ANSWER 107 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1992:84185 Document No. 116:84185 Preparation of radiolabeled proteins for diagnostic or therapeutic use. Gustavson, Linda M.; Srinivasan, Ananthachari; Kasina, Sudhakar; Reno, John M.; Fitzner, Jeffrey N.; **Jones, David S.** (NeoRx Corp., USA). PCT Int. Appl. WO 9109876 A1 19910711, 83 pp. DESIGNATED STATES: RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1990-US7595 19901227. PRIORITY: US 1989-457480 19891229.

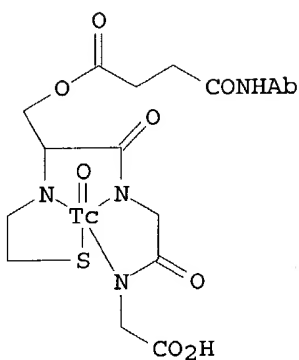
GI



I



II



III

AB Chelating agents [I and II;  $m, p = 0, 1$ ;  $R_1 = H, Me$ ;  $X = O, S$ ;  $X_1 =$  spacer;  $R_3, R_4, R_5 = H, CH_2OH, Me, (CH_2)_nCONH_2, (CH_2)_nCO_2H$ ;  $n = 0-2$ ;  $P =$  targeting mol., conjugation group;  $T, T_1 = H$ , protecting group; one of  $R_6, R_7, R_8 = CHR_1(CH_2)_mXCOX_1P$ , the others  $= H, Me, CH_2OH, (CH_2)_nCONH_2, (CH_2)_nCO_2H$ ], were prepared. Thus, 99mtechnetium chelate III ( $Ab =$  Fab fragment of NRML-05) was prepared in many steps from  $HO_2CCH_2CH_2CO_2Bz$  and  $Z-Ser-OH$  via  $BzO_2C(CH_2)_3OCH_2CH(NHZ)CONHCH_2CONHCH_2CO_2CMe_3$ . The technetium chelates in rats showed reduced localization within the kidneys and intestines.

L19 ANSWER 108 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
1992:99307 Document No. 116:99307 **Conjugates** of biologically stable polymers and polynucleotides for treating systemic lupus erythematosus. Conrad, Michael J.; Coutts, Stephen (La Jolla Pharmaceutical Co., USA). Eur. Pat. Appl. EP 438259 A1 19910724, 23 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1991-300262 19910115. PRIORITY: US 1990-466138 19900116; US 1990-494118 19900313.

AB **Conjugates** of biol. stable polymers, e.g. D-glutamic acid-D-lysine copolymer, and polynucleotide duplexes  $\geq 20$  base pairs that bind human lupus anti-double-stranded DNA autoantibodies are tolerogens for human systemic lupus erythematosus (SLE). D-EK (60:40 mol. ratio; average mol. weight = 30,000 daltons) was conjugated with (AC)30 (preparation given). (TG)30 was then annealed to the **conjugate**. The (TG)30:(AC)30-D-EK **conjugate** was a tolerogen in MRL mice (human SLE animal model).

L19 ANSWER 109 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
1992:51018 Document No. 116:51018 Antitumor activity of Fab' and IgG-anti-CD22 immunotoxins in disseminated human B lymphoma grown in mice with severe combined immunodeficiency disease: effect on tumor cells in extranodal sites. Ghetie, Maria Ana; Richardson, James; Tucker, Thomas; Jones, Diane; Uhr, Jonathan W.; Vitetta, Ellen S. (Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235, USA). Cancer Research, 51(21), 5876-80 (English) 1991. CODEN: CNREA8. ISSN: 0008-5472.

AB The antitumor effects of two anti-CD22 ricin A chain-containing immunotoxin (IT) constructs were compared in mice with severe combined

immunodeficiency disease with human Daudi cell tumors (SCID-Daudi mice). SCID-Daudi mice develop disseminated lymphoma that clin. resembles African Burkitt's lymphoma, i.e., extranodal disease including infiltration of the vertebral column and spinal canal. In the absence of treatment, the mean survival time of SCID-Daudi mice was 45.9 days. The mice were given injections of a dose of IT equal to 40% of the 50% LD. The ITs consisted of either IgG or Fab' fragments of mouse anti-CD22 antibody coupled to deglycosylated ricin A chain (dgA). Both ITs were potent and specific and inhibited protein synthesis in Daudi cells in vitro by 50% at concns. of  $1.2 \times 10^{-12}$  (IgG-dgA) and  $1.3 \times 10^{-11}$ M (Fab'-dgA). When administered to mice beginning 1 day after inoculation with tumor cells, both ITs extended the mean survival time, to 87.2 days (IgG-dgA) or 57.9 days (Fab'-dgA). The latter represented the killing of 2 logs of Daudi cells, and the former 4 logs. IgG antibody alone killed 1 log of tumor cells. The IgG-dgA had an antitumor effect even when administered 20-23 days after tumor inoculation. Gross and histol. examns. of IT-treated tumor-bearing mice showed a marked decrease in the number and size of neoplastic foci in both lymphoid organs and extranodal sites.

L19 ANSWER 110 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 43

91:591011 The Genuine Article (R) Number: GK876. HIGH-POWER BEAM STEERING USING PHASE CONJUGATION THROUGH BRILLOUIN-INDUCED 4-WAVE-MIXING. JONES D C (Reprint); COOK G; RIDLEY K D; SCOTT A M. ROYAL SIGNALS & RADAR ESTAB, ST ANDREWS RD, MALVERN WR14 3PS, WORCS, ENGLAND (Reprint). OPTICS LETTERS (1991) Vol. 16, No. 20, pp. 1551-1553. Pub. country: ENGLAND. Language: ENGLISH.

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB We report an experimental demonstration of a beam-steering concept. A high-reflectivity phase-conjugate mirror is used to steer a high-power phase-conjugate beam using a low-power signal beam. The high-reflectivity phase conjugation is achieved using Brillouin-induced four-wave mixing in a cell containing carbon disulfide.

L19 ANSWER 111 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN 1991:330449 Document No.: PREV199141026999; BR41:26999. PREFERENTIAL UPTAKE OF A FLUORESCENT GLUTATHIONE S-CONJUGATE BY ALVEOLAR TYPE II CELLS IN THE ISOLATED PERFUSED RAT LUNG. BAI C [Reprint author]; BROWN L A; JONES D P. DEP BIOCHEMISTRY, EMORY UNIV SCH MED, ATLANTA, GA 30322, USA. FASEB Journal, (1991) Vol. 5, No. 6, pp. A1489. Meeting Info.: 75TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ATLANTA, GEORGIA, USA, APRIL 21-25, 1991. FASEB (FED AM SOC EXP BIOL) J. CODEN: FAJOEC. ISSN: 0892-6638. Language: ENGLISH.

L19 ANSWER 112 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN 91:203527 The Genuine Article (R) Number: FE557. PREFERENTIAL UPTAKE OF A FLUORESCENT GLUTATHIONE S-CONJUGATE BY ALVEOLAR TYPE-II CELLS IN THE ISOLATED PERFUSED RAT LUNG. BAI C (Reprint); BROWN L A; JONES D P. EMORY UNIV, SCH MED, DEPT BIOCHEM, ATLANTA, GA, 30322; EMORY UNIV, SCH MED, DEPT PEDIAT, ATLANTA, GA, 30322. FASEB JOURNAL (1991) Vol. 5, No. 6, pp. A1489. Pub. country: USA. Language: ENGLISH.

L19 ANSWER 113 OF 161 MEDLINE on STN DUPLICATE 44 91337159. PubMed ID: 1872890. Effect of chronic hypoxia on acetaminophen metabolism in the rat. Aw T Y; Shan X Q; Sillau A H; Jones D P. (Department of Biochemistry, Emory University School of Medicine, Atlanta, GA 30322. ) Biochemical pharmacology, (1991 Aug 8) 42 (5) 1029-38. Journal code: 0101032. ISSN: 0006-2952. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The effect of chronic hypoxia (10.5% O2 for 8-9 days) on acetaminophen metabolism was studied in vivo or in isolated cell or microsomal systems. Results from in vivo studies with oral administration of acetaminophen showed that in hypoxic rats, the plasma appearance of the drug was delayed and the plasma half-life was increased. Analyses of the area under the

curve (AUC<sub>oral</sub>) showed that this value was higher in hypoxic rats, whereas the rate constants for elimination ( $k_{elim}$ ) and absorption ( $k_{abs}$ ) were lower in these animals. Formation of the glucuronide and sulfate **conjugates** was decreased significantly ( $P$  less than 0.05) in hypoxic animals. The calculated volume of distribution ( $V_d$ ) after an intravenous dose was not different in either group but total clearance ( $CL$ ) was 35% lower in hypoxic rats. Studies with isolated hepatocytes from both groups revealed that glucuronidation and sulfation were inhibited markedly at low  $O_2$  concentrations. The  $O_2$  concentrations required for half-maximal production ( $P_{50}$  values) of glucuronide (2.3  $\mu M$   $O_2$ ) and sulfate (1.8  $\mu M$   $O_2$ ) **conjugates** in cells from hypoxic animals were lower than for control cells (5.3  $\mu M$  and 3.9  $\mu M$   $O_2$  for glucuronide and sulfate **conjugates**, respectively). Maximal rates of conjugation in cells from hypoxic rats were 60-70% of control rates. Similar decreases in microsomal UDP-glucuronosyltransferase and cytosolic sulfotransferase activities were found in livers of animals exposed to chronic hypoxia. These lower  $P_{50}$  values are consistent with a lower  $P_{50}$  for oxidation of mitochondrial cytochromes in hypoxic cells. In comparison, the  $P_{50}$  for glutathione conjugation (4.1  $\mu M$   $O_2$ ) was not statistically different from control (4.6  $\mu M$   $O_2$ ), but the maximal rate was 65% higher. The results show that chronic hypoxia causes a change of absorptive processes and decreased glucuronidation and sulfation reactions which affects the disposition of acetaminophen and potentially the disposition of a variety of other exogenous and endogenous compounds.

L19 ANSWER 114 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 45

1992:258513 Document No.: PREV199293134838; BA93:134838. PROFILE OF EMBRYONIC ECDYSTEROIDS IN THE DECAPOD CRUSTACEAN MACROBRACHIUM-ROSENBERGII. YOUNG N J [Reprint author]; WEBSTER S G; JONES D A; REES H H. DEP BIOCHEM, UNIV LIVERPOOL, PO BOX 147, LIVERPOOL L69 3BX, UK. Invertebrate Reproduction and Development, (1991) Vol. 20, No. 3, pp. 201-212. CODEN: IRDEE2. ISSN: 0792-4259. Language: ENGLISH.

AB The ecdysteroid composition of embryos of *M. rosenbergii* at various stages of embryogenesis has been studied by means of radioimmunoassay (RIA), high-performance liquid chromatography-RIA (HPLC-RIA) and gas chromatography/mass spectrometry (selected ion monitoring; GC/MS(SIM)). In newly-laid eggs, only free ecdysteroids (ecdysone and 20-hydroxyecdysone) were detected, whereas eggs at an early stage of embryogenesis contained ecdysone and also low levels of apolar ecdysteroid **conjugates**. Mid stage embryonating eggs contained comparatively high levels of both free ecdysteroid (ecdysone, 18.3ng/g) and apolar **conjugates** (20.9ng/g). Late embryos contained by far the highest overall level of ecdysteroid, indicating the ability of the developing embryo to synthesize ecdysteroid. In contrast to the other stages, late embryos contained 26-hydroxyecdysone, ecdysoneic acid and 20-hydroxyecdysoneic acid at relatively low levels and 2,3-diacetylcyclopentyl 22-phosphate at a comparatively high level (324.0 ng/g). These results suggest that the developing embryo of *M. rosenbergii* is capable of both ecdysteroid biosynthesis (presumably for utilization during specific stages of embryogenesis), conversion into apolar **conjugates** and inactivation by conversion into 26-oic acids and polar **conjugates**.

L19 ANSWER 115 OF 161 MEDLINE on STN DUPLICATE 46  
91378519. PubMed ID: 1654841. Immunochemical study of subunit VI (Mr 13,400) of mitochondrial ubiquinol-cytochrome c reductase. Usui S; Yu L; Harmon J; Yu C A. (Department of Biochemistry, Oklahoma State University, Stillwater 74078. ) Archives of biochemistry and biophysics, (1991 Aug 15) 289 (1) 109-17. Journal code: 0372430. ISSN: 0003-9861. Pub. country: United States. Language: English.

AB A preparation containing the Mr 13,400 protein (subunit VI), phospholipid, and ubiquinone was isolated from bovine heart mitochondrial ubiquinol-cytochrome c reductase by a procedure involving Triton X-100 and



urea solubilization, calcium phosphate-cellulose column chromatography at different pHs, acetone precipitation, and decanoyl-N-methylglucamide-sodium cholate extraction. The protein in this preparation corresponds to subunit VI of ubiquinol-cytochrome c reductase resolved in the sodium dodecyl sulfate-polyacrylamide gel electrophoresis system of Schagger et al. (1987, FEBS Lett. 21, 161-168) and has the same amino acid sequence as that of the Mr 13,400 protein reported by Wakabayashi et al. (1985, J. Biol. Chemical 260, 337-343). The phospholipid and ubiquinone present in the preparation copurify with but are not intrinsic components of, the Mr 13,400 protein. This preparation has a potency and behavior identical to that of a free phospholipid preparation in restoring activity to delipidated ubiquinol-cytochrome c reductase. Antibodies against Mr 13,400 react only with Mr 13,400 protein and complexes which contain it. They do not inhibit intact, lipid-sufficient ubiquinol-cytochrome c reductase. However, when delipidated ubiquinol-cytochrome c reductase is incubated with antibodies prior to reconstitution with phospholipid, a 55% decrease in the restoration activity is observed, indicating that the catalytic site-related epitopes of the Mr 13,400 protein are buried in the phospholipid environment. Antibodies against Mr 13,400 cause an increase of apparent Km for ubiquinol-2 in ubiquinol-cytochrome c reductase. When mitoplasts or submitochondrial particles are exposed to a horseradish peroxidase conjugate of the Fab' fragment of anti-Mr 13,400 antibodies, peroxidase activity is found mainly in the submitochondrial particles preparation; little activity is detected in mitoplasts. This suggests that the Mr 13,400 protein is extruded toward the matrix side of the membrane.

L19 ANSWER 116 OF 161 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 47

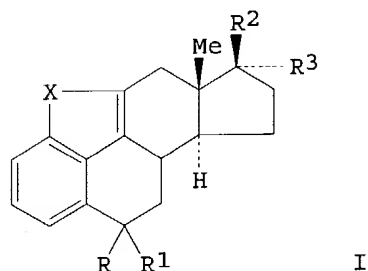
90173037 EMBASE Document No.: 1990173037. The small molecular mass ubiquinone-binding protein (QPc-9.5 kDa) in mitochondrial ubiquinol-cytochrome c reductase: Isolation, ubiquinone-binding domain, and immunoinhibition. Usui S.; Yu L.; Yu C.-A.. Department of Biochemistry, OAES, Oklahoma State University, Stillwater, OK 74078, United States. Biochemistry 29/19 (4618-4626) 1990. ISSN: 0006-2960. CODEN: BICHAW. Pub. Country: United States. Language: English. Summary Language: English.

AB The small molecular mass ubiquinone-binding protein (QPc-9.5 kDa) was purified to homogeneity from 3-azido-2-methyl-5-methoxy-6-(3,7-dimethyl[3H]octyl)-1,4-benzoquinol- labeled bovine heart mitochondrial ubiquinol-cytochrome c reductase. The N-terminal amino acid sequence of the isolated protein is Gly-Arg-Gln-Phe-Gly-His-Leu-Thr-Arg-Val-Arg-His-, which is identical with that of a M(r) = 9500 protein in the reductase [Borchart et al. (1986) FEBS Lett. 200, 81-86]. A ubiquinone-binding peptide was prepared from [3H]azidoubiquinol-labeled QPc-9.5 kDa protein by trypsin digestion followed by HPLC separation. The partial N-terminal amino acid sequence of this peptide, Val-Ala-Pro-Pro-Phe-Val-Ala-Phe-Tyr-Leu-, corresponds to amino acid residues 48-57 in the reported M(r) = 9500 protein. According to the proposed structural model for the M(r) = 9500 protein, the azido-Q-labeled peptide is located in the membrane on the matrix side. These results confirm our previous assessment that the M(r) = 13400 subunit is not the small molecular weight Q-binding protein. Purified antibodies against QPc-9.5 kDa have a higher titer with isolated QPc-9.5 kDa protein and complexes that contain it. Although antibodies against QPc-9.5 kDa do not inhibit intact succinate- and ubiquinol-cytochrome c reductases, a decrease of 85% and 20% in restoration of succinate and ubiquinol-cytochrome c reductases, respectively, is observed when delipidated succinate- or ubiquinol-cytochrome reductases are incubated with antibodies prior to reconstitution with ubiquinone and phospholipid, indicating that epitopes at the catalytic site of QPc-9.5 kDa are buried in the phospholipid environment. Antibodies against QPc-9.5 kDa cause an increase of the apparent K(m) for ubiquinol 2 in ubiquinol-cytochrome c reductase, suggesting that the low level of inhibition of the reductase by these antibodies may be due to the use of excess ubiquinol 2 in the assay

mixture. Since antibodies against QPc-9.5 kDa inhibit 75% of the antimycin-sensitive plastoquinone reduction activity in the reconstituted succinate-cytochrome c reductase, QPc-9.5 kDa may be involved in the Q(i) site. The topological arrangement of QPc-9.5 kDa in the mitochondrial membrane was examined immunologically with an anti-QPc-9.5 kDa Fab' fragment-horseradish peroxidase **conjugate**. When intact mitochondria (mitoplasts) or electron-transport particles (ETP) are exposed to this **conjugate**, peroxidase activity is found in both preparations, with ETP having the higher activity. This suggests that QPc-9.5 kDa is transmembranous, possibly with more mass on the matrix side of the membrane.

L19 ANSWER 117 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 1990:631757 Document No. 113:231757 Short convergent syntheses of 1,11-epithio and 1,11-epoxy steroids. Adams, Joseph P.; Bowler, Jean; Collins, Mark A.; **Jones, D. Neville**; Swallow, Steven (Dep. Chem., Univ. Sheffield, Sheffield, S3 7HF, UK). Tetrahedron Letters, 31(30), 4355-8 (English) 1990. CODEN: TELEAY. ISSN: 0040-4039. OTHER SOURCES: CASREACT 113:231757.

GI



AB Three component coupling of allyl aryl sulfones with 2-methylcyclopentenone and 2-(bromomethyl)benzo[b]thiophene or its furan analog, followed by intramol. Lewis acid catalyzed cyclizations provided short stereoselective syntheses of 1,11-epithio and 1,11-epoxy steroids I (R = R1 = Me, R2R3 = O; X = O, S; RR1 = O, R2 = OH, R3 = H, X = S).

L19 ANSWER 118 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 1990:185666 Document No. 112:185666 Application of target-specific drug immunoconjugates to experimental bone marrow replacement therapy in mice. Ding, Lei; **Yu, Lizhang**; Xie, Shusheng; Gong, Donger; Vergidis, Rucy; Diener, Erwin (Dep. Immunol., Univ. Alberta, Edmonton, AB, T6G 2H7, Can.). Cancer Research, 50(5), 1538-43 (English) 1990. CODEN: CNREA8. ISSN: 0008-5472.

AB The cytotoxic drug daunomycin attached via an acid-sensitive spacer to monoclonal antibody of appropriate specificity was shown to purge murine bone marrow of contaminating tumor cells without affecting its hematopoietic potential. Lethally irradiated mice reconstituted with syngeneic bone marrow from which contaminating lymphoma cells had been removed survived indefinitely. Furthermore, lymphoma-bearing mice, provided they were sufficiently irradiated to eliminate tumor cells in situ, were successfully reconstituted with fully allogeneic bone marrow from which potentially graft-vs.-host-reactive T-cells had been purged.

L19 ANSWER 119 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE  
 48

90:493439 The Genuine Article (R) Number: DX057. 3-WAVE AND 4-WAVE FORWARD PHASE-**CONJUGATE** IMAGING IN PHOTOREFRACTIVE BISMUTH SILICON-OXIDE. **JONES D C (Reprint)**; LYUKSYUTOV S F; SOLYMAR L. UNIV OXFORD, DEPT ENGN SCI, HOLOG GRP, OXFORD OX1 3PJ, ENGLAND (Reprint). OPTICS LETTERS (1990) Vol. 15, No. 17, pp. 935-937. Pub. country: ENGLAND.

Language: ENGLISH.

- L19 ANSWER 120 OF 161 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 49  
91032679 EMBASE Document No.: 1991032679. Asymmetric synthesis of homochiral dibenzylbutyrolactone lignans by **conjugate** addition to a chiral butenolide. Pelter A.; Ward R.S.; **Jones D.M.**; Maddocks P.. Chemistry Department, University College, Singleton Park, Swansea SA2 8PP, United Kingdom. Tetrahedron Asymmetry 1/12 (857-860) 1990. ISSN: 0957-4166. CODEN: TASYE3. Pub. Country: United Kingdom. Language: English. Summary Language: English.
- AB Addition of sulphur stabilised carbanions to a chiral non-racemic butenolide followed by reaction with an aromatic aldehyde affords a short synthesis of homochiral dibenzylbutyrolactone derivatives. Desulphurisation of the first formed adducts proceeds in almost quantitative yield to afford the parent lignan.
- L19 ANSWER 121 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
91:19849 The Genuine Article (R) Number: EQ333. ASYMMETRIC-SYNTHESIS OF HOMOCHIRAL DIBENZYL BUTYROLACTONE LIGNANS BY **CONJUGATE** ADDITION TO A CHIRAL BUTENOLIDE. PELTER A (Reprint); WARD R S; **JONES D M** ; MADDOCKS P. UNIV COLL SWANSEA, DEPT CHEM, SINGLETON PK, SWANSEA SA2 8PP, W GLAM, WALES (Reprint); WELLCOME FDN LTD, DARTFORD, KENT, ENGLAND. TETRAHEDRON-ASYMMETRY (1990) Vol. 1, No. 12, pp. 857-860. Pub. country: WALES; ENGLAND. Language: ENGLISH.  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*
- AB Addition of sulphur stabilised carbanions to a chiral non-racemic butenolide followed by reaction with an aromatic aldehyde affords a short synthesis of homochiral dibenzylbutyrolactone derivatives. Desulphurisation of the first formed adducts proceeds in almost quantitative yield to afford the parent lignan.
- L19 ANSWER 122 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
1990:413913 Document No.: PREV199090074714; BA90:74714. CHARACTERISTICS OF THE NOPALINE CATABOLIC PLASMID IN AGROBACTERIUM STRAINS K84 AND K1026 USED FOR BIOLOGICAL CONTROL OF CROWN GALL DISEASE. CLARE B G [Reprint author]; KERR A; **JONES D A.** DEP PLANT PATHOL, UNIV ADELAIDE, WAITE AGRIC RES INST, GLEN OSMOND, SOUTH AUST, 5064, AUST. Plasmid, (1990) Vol. 23, No. 2, pp. 126-137.  
CODEN: PLSMDX. ISSN: 0147-619X. Language: ENGLISH.
- AB Wild-type Agrobacterium radiobacter strains 84 and its Tra- derivative K1026, used for biological control of crown gall disease, each contain the plasmid pAtK84b. It confers incompatibility to tumor-inducing (Ti) plasmids of pathogenic A. tumefaciens, thus preventing transfer of Ti plasmids into K84 and K1026, and the consequent development of pathogens resistant to the specific antibiotic, agrocin 84 produced by K84 and K1026. pAtK84b also resembles one group of Ti plasmids in its capacity for directing nopaline catabolism. A study of the DNA homology among pAtK84b, pTiC58, and pTiAch5 was carried out. pAtK84b was transferred by conjugation to a plasmidless recipient and, after isolation, was hybridized with Ti plasmid DNA. Areas of DNA homology were located on published maps of pTiC58 and pTiAch5, a restriction enzyme map of pAtK84b was constructed, and areas of homology with DNA of known genetic function were located on the map. Strong and extensive (over 50%) homology was found between pAtK84b and pTiC58 (nopaline catabolic, Noc), but much less between pAtK84b and pTiAch5 (octopine catabolic). There was no detectable homology between pAtK84b and the oncogenic T-DNA and virulence (Vir) regions of either Ti plasmid. The size of pAtK84b was 173 kb and the orientation of regions of identified gene function (Noc, incompatibility/origin of replication, and conjugal transfer) on pTiC58 was matched by the locations of homologous areas on pAtK84b. It is concluded that pAtK84b may be a deletion product of a pTiC58-type plasmid which has been disarmed in the oncogenic T-DNA and Vir regions.
- L19 ANSWER 123 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1991:237133 Document No. 114:237133 Bipolaronic enhanced third order nonlinearity in organic ladder polymers. Cao, X. F.; Jiang, J. P.; Hellwarth, R. W.; Yu, L. P.; Chen, M.; Dalton, L. (Dep. Electr. Eng. Phys., Univ. South. California, Los Angeles, CA, 90089-0484, USA). Proceedings of SPIE-The International Society for Optical Engineering, 1337(Nonlinear Opt. Prop. Org. Mater. 3), 114-24 (English) 1990. CODEN: PSISDG. ISSN: 0277-786X.

AB Third order nonlinear optical properties of organic ladder copolymer (POL) system was studied using degenerate 4-wave mixing with ps laser pulse. Both the real and imaginary part of the 3rd order nonlinear susceptibility  $\chi(3)$  were determined by a new phase **conjugate** interferometric method over  $\lambda = 532-720$  nm. From the space symmetry and wavelength dependence of  $\chi(3)$ , the observed nonlinearity was attributed to the nonlinear photoexcitation of bipolaron states in this ladder copolymer system.

L19 ANSWER 124 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1991:30208 Document No. 114:30208 Preparation of chelating agents for metal radionuclides, usable as radiotherapeutic and radiodiagnostic **conjugates**. Fritzberg, Alan R.; Srinivasan, Ananthachari; Jones, David S.; Wilkening, David W. (NeoRx Corp., USA). Eur. Pat. Appl. EP 344724 A2 19891206, 49 pp. DESIGNATED STATES: R: DE, FR, GB, IT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1989-109756 19890530. PRIORITY: US 1988-201134 19880531.

GI For diagram(s), see printed CA Issue.

AB The chelating agents I ( $X_1, X_2, X_3, X_4 = H, O$ ;  $X_1 \neq X_2 = O$ ;  $X_3 \neq X_4 = O$ ; A, A1 = H, C1-6 alkyl, CH<sub>2</sub>CH<sub>2</sub>SR, COCH<sub>2</sub>SR; when  $X_1$  or  $X_2 = O$ , A = H; when  $X_3$  or  $X_4 = O$ , then A1 = H; Y, Y1 = H, CH<sub>2</sub>SR1; R, R1, R2R4 = S-protecting group; Q = H, polar group; Z = Wm R4; W = CH<sub>2</sub>, CH<sub>2</sub>O, CH<sub>2</sub>CO; m = 0-5; R4 = reactive group; when Z is attached to C- $\alpha$ , there is either no  $X_1$  or no Q at C- $\alpha$ ; when Z is attached to C- $\beta$ , there is either no  $X_3$  or no Q at C- $\beta$ ; when  $X_1 = O$ , there is no Z at C- $\alpha$ ; when  $X_3 = O$ , there is no Z at C- $\beta$ ) and related compds. are prepared I are chelating <sup>99m</sup>Tc, <sup>186</sup>/188Re and other radionuclides, and the chelates are conjugated to antibodies, peptides, hormones, enzymes, etc., for targeting in radiodiagnosis and radiotherapy. A solution of 4,5-diaminopentanoic acid (preparation given) in DMF was treated with Et<sub>3</sub>N and succinimidyl 2,3-bis(mercaptoisobutyryl)propionate, to give bis-4,5-(2',3'-mercaptoisobutyryl)propionamidopentanoic acid, which, in THF, was treated with N,N'-dicyclohexylcarbodiimide and N-hydroxysuccinimide, to yield succinimidyl bis-4,5-(2',3'-mercaptoisobutyryl)propionamidopentanoate. This was reacted with <sup>99m</sup>Tc-gluconate complex (preparation given), in HCl-containing iso-PrOH-HAcO to give the corresponding chelate, which was conjugated with a monoclonal antibody, as usual.

L19 ANSWER 125 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1989:546392 Document No. 111:146392 Specific killing effect of monoclonal antibody-conjugated daunomycin against colorectal tumor. Yu, Lizhang; Diener, Erwin (Inst. Urol., Beijing Med. Univ., Beijing, Peop. Rep. China). Zhonghua Weishengwuxue He Mianyixue Zazhi, 9(3), 156-60 (Chinese) 1989. CODEN: ZWMZDP. ISSN: 0254-5101.

AB Daunomycin coupled from a pH-sensitive spacer, cisaconytal, with monoclonal antibodies to human colorectal adenocarcinoma Lovo cells had specific killing effect on the colorectal tumor in vitro and in nude mice in vivo.

L19 ANSWER 126 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

1989:300052 Document No.: PREV198937014429; BR37:14429. GLUTATHIONE HOMEOSTASIS AND GLUTATHIONE S-**CONJUGATE** TOXICITY IN THE KIDNEY. LASH L H [Reprint author]; ANDERS M W; JONES D P. DEP PHARMACOL, UNIV ROCHESTER SCH MED AND DENT, ROCHESTER, NY 14642, USA. Rev. Biochem. Toxicol., (1988) pp. 29-68. HODGSON, E., J. R. BEND AND R. M. PHILPOT (ED.). REVIEWS IN BIOCHEMICAL TOXICOLOGY, VOL. 9. XVII+347P. ELSEVIER SCIENCE PUBLISHING CO., INC.: NEW YORK, NEW YORK, USA; AMSTERDAM,

NETHERLANDS. ILLUS. Publisher: Series: Reviews in Biochemical Toxicology.  
CODEN: RBTODU. ISSN: 0163-7673. ISBN: 0-444-01321-0. Language: ENGLISH.

L19 ANSWER 127 OF 161 MEDLINE on STN  
88254577. PubMed ID: 3289886. An enzyme-linked immunosorbent assay (ELISA) for detection of antibodies against swine fever virus using horseradish-peroxidase-protein-A as **conjugate**. Yu L; Liu J H; Shao M F; Li X M; Zhang X M. DTW. Deutsche tierärztliche Wochenschrift, (1988 Mar) 95 (3) 106-7. Journal code: 7706565. ISSN: 0341-6593. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: English.

L19 ANSWER 128 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
88:149585 The Genuine Article (R) Number: M4593. AN ENZYME-LINKED IMMUNOSORBENT-ASSAY (ELISA) FOR DETECTION OF ANTIBODIES AGAINST SWINE FEVER VIRUS USING HORSERADISH-PEROXIDASE-PROTEIN-A AS **CONJUGATE**. YU L (Reprint); LIU J H; SHAO M F; LI X M; ZHANG X M. ZHEJIANG AGR UNIV, DEPT ANIM HUSB & VET MED, ZHEJIANG, PEOPLES R CHINA (Reprint); INST IMMUNOREAGENTS, NING BOU, PEOPLES R CHINA. DEUTSCHE TIERARZTLICHE WOCHENSCHRIFT (1988) Vol. 95, No. 3, pp. 106-107. Pub. country: PEOPLES REPUBLIC OF CHINA. Language: ENGLISH.

L19 ANSWER 129 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
1987:375231 Document No.: PREV198733065706; BR33:65706. SYNTHESIS AND RADIOIODINATION OF IODOPHENYL **CONJUGATES** FOR PROTEIN LABELING. HYLARIDES M [Reprint author]; JONES D; SEUBERT J; HADLEY S; WILBUR S. NEORX CORP, SEATTLE, WASH, USA. Journal of Nuclear Medicine, (1987) Vol. 28, No. 4 SUPPL, pp. 560. Meeting Info.: 34TH ANNUAL MEETING OF THE SOCIETY OF NUCLEAR MEDICINE, TORONTO, ONTARIO, CANADA, JUNE 2-5, 1987. J NUCL MED. CODEN: JNMEAQ. ISSN: 0161-5505. Language: ENGLISH.

L19 ANSWER 130 OF 161 MEDLINE on STN DUPLICATE 50  
87303861. PubMed ID: 3622319. Diagnosis and therapy of neuroectodermally associated tumours using targeted radiation. Kemshead J T; Lashford L S; Jones D H; Coakham H B. Developmental neuroscience, (1987) 9 (2) 69-83. Journal code: 7809375. ISSN: 0378-5866. Pub. country: Switzerland. Language: English.

AB Monoclonal antibodies have been proposed as targeting agents for cytotoxic compounds in vivo. We have undertaken a phase 1 study of <sup>131</sup>I UJ13A in patients with neuroblastoma as well as a pilot study for the intrathecal use of radiolabelled **conjugates** for diffuse malignant meningitis. Access to solid tumour deposits appears to be a major problem in targeting sufficient isotope to elicit a therapeutic response. This, however, is overcome in the intrathecal use of antibodies for diffuse disease. Problems have also been identified in changes in the pharmacokinetics of antibody handling that occur on repeated administration of **conjugate** to patient. This is presumably due to the generation of an anti-mouse Ig response. These studies indicate some of the limitations in using murine antibodies as targeting agents and point to areas where their use may be of maximal effect.

L19 ANSWER 131 OF 161 MEDLINE on STN  
87144692. PubMed ID: 3821919. Therapeutic application of radiolabeled monoclonal antibody UJ13A in children with disseminated neuroblastoma. Lashford L; Jones D; Pritchard J; Gordon I; Breatnach F; Kemshead J T. NCI monographs : a publication of the National Cancer Institute, (1987) (3) 53-7. Journal code: 8610384. ISSN: 0893-2751. Pub. country: United States. Language: English.

AB Dosimetric data from UJ13A scanning studies using <sup>131</sup>I are presented for children with stage IV neuroblastoma and primary brain tumor. The data demonstrate a large variation among patients in dose delivery to vulnerable organs and tumors. Against this background, a phase I toxicity study is under way with escalating amounts of **conjugate** administered to patients who have stage IV neuroblastoma. Major toxicity

has been confined to bone marrow aplasia and necessitates bone marrow harvest prior to therapy. Specific problems encountered include altered kinetics during therapy following tracer studies and adequate dose delivery in large tumor masses.

L19 ANSWER 132 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1987:152571 Document No. 106:152571 Preparation of radiohalogenated small molecules for protein labeling and their use in biodistribution studies and kits. Wilbur, Daniel Scott; Fritzberg, Alan Richard; **Jones, David Schuster** (NeoRx Corp., USA). Eur. Pat. Appl. EP 203764 A2 19861203, 26 pp. DESIGNATED STATES: R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1986-303757 19860516. PRIORITY: US 1985-735392 19850517; US 1986-852740 19860421.

AB A rapid and efficient method of introducing high specific activity halogen radionuclides into nonactivated aromatic rings of small mols. that can be conjugated to proteins under conditions that preserve the biol. activity of the protein is given. These radiohalogenated small mols., having formulas of of XArR (X = radioisotope of I, Br, F, At; Ar = aromatic, heteroarom. ring; R = short-chain substituent that does not highly activate the ring and that has a functional group suitable for conjugation to protein) or MArR [M = Sn(n-Bu)<sub>3</sub>, SnMe<sub>3</sub>, HgX<sub>2</sub> (X = Cl, Br, I), HgOAc, B(OH)<sub>2</sub>, BZ<sub>3</sub> (Z = alkyl, alkoxy); Ar, R, as defined above], provide radiolabeled proteins with greater stability than prior art substitutions onto activated aromatic rings such as phenols. When the radiohalogen is substituted in p or m positions on an aromatic ring without a hydroxyl group, the radiolabel is less susceptible to attack by deiodinase enzymes. Tri-n-butylstannyl 4-(tri-n-butylstannyl)benzoate (I) was prepared by reacting 4-bromobenzoic acid with n-BuLi followed by metalation with Sn(n-Bu)<sub>3</sub>Cl. I was activated for protein conjugation by reaction with dicyclohexylcarbodiimide and N-hydroxysuccinimide. The product N-succinimidyl 4-(tributylstannyl)benzoate was radiohalogenated with Na <sup>125</sup>I before reaction with an antibody. The labeled antibody was used in biodistribution studies.

L19 ANSWER 133 OF 161 MEDLINE on STN

DUPLICATE 51

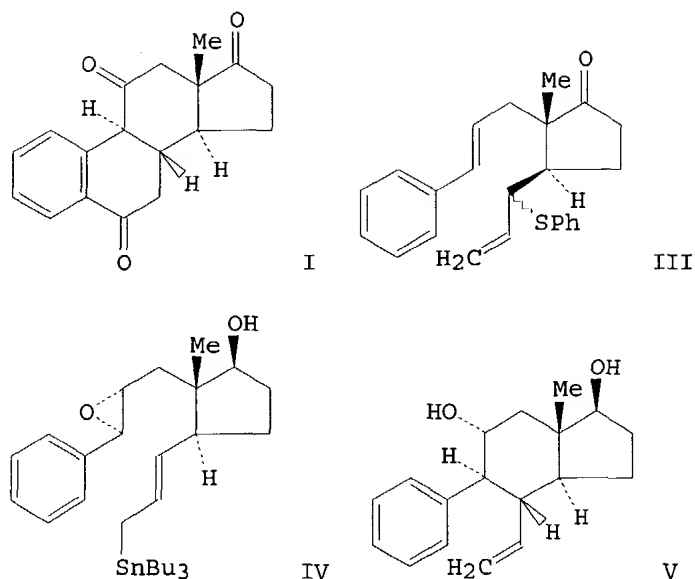
87081762. PubMed ID: 3792998. The use of nonradiolabelled steroid infusions to investigate the origin of oestrone sulphate in postmenopausal women. Reed M J; Noel C T; **Jones D L**; Jacobs H S; Scanlon M J; James V H. Hormone and metabolic research. Hormon- und Stoffwechselforschung. Hormones et metabolisme, (1986 Nov) 18 (11) 779-83. Journal code: 0177722. ISSN: 0018-5043. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: English.

AB Infusion of nonradiolabelled dehydroepiandrosterone sulphate (DHA-S) has been used to investigate the possible formation of oestrone sulphate via a sulphated **conjugate** of androstenedione. The metabolic clearance rate (MCR) of DHA-S also was measured and the mean value (25 1/24h) was similar to values reported using isotopic techniques. Although conversion of DHA-S to 5-androstenediol, a steroid with oestrogenic properties, was detected during infusion of DHA-S, there were no significant increases in plasma levels of conjugated androstenedione or oestrone sulphate. The MCR's oestrone sulphate measured using infusion of nonradiolabelled steroid in two menopausal women were 99 1/24h and 121 1/24h. For one woman, the production rate of oestrone sulphate, calculated from the conversion of oestrone and oestradiol to oestrone sulphate (151 nmol/day) was similar to the measured production rate of oestrone sulphate (144 nmol/day). It is concluded that in menopausal women, oestrone sulphate is derived from conversion of oestrone and oestradiol with no formation occurring via conjugated androstenedione.

L19 ANSWER 134 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1986:460801 Document No. 105:60801 A simple stereoselective steroid synthesis: cyclization of an epoxystannane. **Jones, D. Neville**; Peel, Michael R. (Dep. Chem., Univ. Sheffield, Sheffield, S3 7HF, UK). Journal of the Chemical Society, Chemical Communications (3), 216-17 (English) 1986. CODEN: JCCCAT. ISSN: 0022-4936. OTHER SOURCES: CASREACT

GI

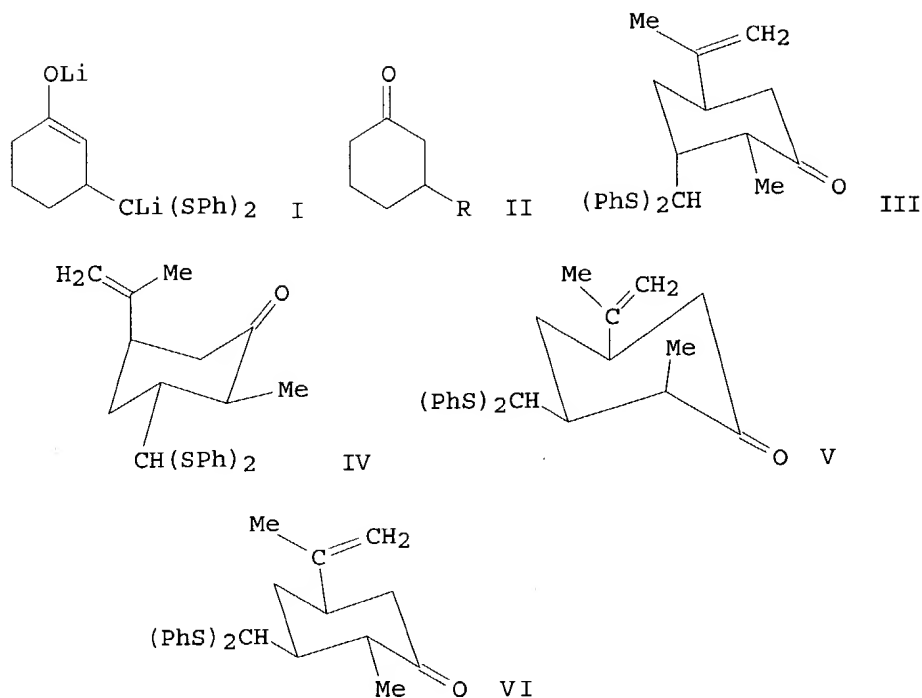


AB The estratrienetrione I was prepared from 2-methylcyclopent-2-enone (II) in 7 steps. The key steps were the **conjugate** addition of  $\text{H}_2\text{C}:\text{CHCH}_2\text{SPh}$  with II and stereoselective alkylation of the resulting adduct with  $\text{PhCH}:\text{CHCH}_2\text{Br}$  to give 53% III, and the stereoselective acid-catalyzed cyclization of the epoxy allyl stannane IV to give 62% V.

L19 ANSWER 135 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN 85:495305 The Genuine Article (R) Number: AQD15. FORMATION AND USES OF THE DIANION FORMALLY PRODUCED BY **CONJUGATE** ADDITION OF BIS(PHENYLTHIO)METHYL DIANION TO CYCLOHEX-2-EN-1-ONE - CONFIGURATIONS AND CONFORMATIONS OF THE PRODUCTS OF **CONJUGATE** ADDITION OF TRIS(PHENYLTHIO)METHYLLITHIUM TO CARVONE. COHEN T (Reprint); YU L C. UNIV PITTSBURGH, DEPT CHEM, PITTSBURGH, PA, 15260 (Reprint). JOURNAL OF ORGANIC CHEMISTRY (1985) Vol. 50, No. 18, pp. 3266-3269. Pub. country: USA. Language: ENGLISH.

L19 ANSWER 136 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN 1985:560703 Document No. 103:160703 Formation and uses of the dianion formally produced by **conjugate** addition of bis(phenylthio)methyl dianion to cyclohex-2-en-1-one. Configurations and conformations of the products of **conjugate** addition of tris(phenylthio)methyl lithium to carvone. Cohen, Theodore; Yu, Lin Chen (Dep. Chem., Univ. Pittsburgh, Pittsburgh, PA, 15260, USA). Journal of Organic Chemistry, 50(18), 3266-9 (English) 1985. CODEN: JOCEAH. ISSN: 0022-3263. OTHER SOURCES: CASREACT 103:160703.

GI



AB Treating 2-cyclohexen-1-one with  $(\text{PhS})_3\text{CLi}$  followed by  $\text{MeCHLi}:\text{Et}$  gave the enolate thioacetal dianion I which reacted with electrophiles, e.g.,  $\text{PhCHO}$ ,  $\text{H}_2\text{O}$ , or  $\text{MeI}$ , followed by quenching with  $\text{H}_2\text{O}$  to give 71, 75, and 88% cyclohexanones II [ $\text{R} = \text{C}(\text{SPh})_2\text{CH}(\text{OH})\text{Ph}$ ,  $\text{CH}(\text{SPh})_2$ ,  $\text{C}(\text{SPh})_2\text{Me}$ ], resp. Similarly (-)-carvone gave 3 stereoisomers III, IV, and V when quenched with aqueous  $\text{AcOH}$  and an addnl. stereoisomer VI when quenched with water.

L19 ANSWER 137 OF 161 MEDLINE on STN DUPLICATE 52  
85233503. PubMed ID: 4008099. Therapeutic application of a radiolabelled monoclonal antibody in nude mice xenografted with human neuroblastoma: tumoricidal effects and distribution studies. Jones D H; Goldman A; Gordon I; Pritchard J; Gregory B J; Kemshead J T. International journal of cancer. Journal international du cancer, (1985 Jun 15) 35 (6) 715-20. Journal code: 0042124. ISSN: 0020-7136. Pub. country: United States. Language: English.

AB Monoclonal antibody UJ13A radiolabelled with isotopes of iodine has been shown to selectively localize to human neuroblastoma xenografts. When  $^{131}\text{I}$ -UJ13A conjugates were given to nude mice at high doses (100-150 microCi), tumours temporarily disappeared, only to regrow. No selection for neuroblastoma cells that were UJ13A - negative was observed. Distribution studies on mice receiving radiolabelled UJ13A demonstrated the antibody is rapidly lost from the blood of animals. This cannot be accounted for by selective uptake into xenografts or any other mouse organ examined. We concluded there is a rapid equilibration of isotope between intra- and extravascular spaces in the animal. The rapid, biphasic loss of UJ13A from the blood of mice may explain why so little injected antibody can target to the human tumour xenografts.

L19 ANSWER 138 OF 161 MEDLINE on STN DUPLICATE 53  
85295901. PubMed ID: 3839897. Uptake of the glutathione conjugate S-(1,2-dichlorovinyl)glutathione by renal basal-lateral membrane vesicles and isolated kidney cells. Lash L H; Jones D P. Molecular pharmacology, (1985 Sep) 28 (3) 278-82. Journal code: 0035623. ISSN: 0026-895X. Pub. country: United States. Language: English.

AB Transport of the glutathione S-conjugate, S-(1,2-dichlorovinyl)glutathione (DCVG), was studied in renal basal-lateral



membrane vesicles and isolated rat kidney cells. The time course of S-(1,2-dichlorovinyl)glutathione uptake in membrane vesicles exhibited an overshoot in the presence of sodium, indicating transport against a concentration gradient. The initial rate of uptake with membrane potential clamped at 0 mV was stimulated 2.5-fold by an inwardly directed gradient of 100 mM sodium chloride. Hyperpolarization of the membrane potential to -60 mV in the presence of sodium stimulated uptake another 2.7-fold, indicating that cotransport of sodium and S-(1,2-dichlorovinyl)glutathione is electrogenic. Sodium-dependent DCVG uptake was inhibited by glutathione, glutathione disulfide, and gamma-glutamylglutamate, but not by the corresponding cysteine S-**conjugate**, S-(1,2-dichlorovinyl)cysteine, indicating that the transport system is specific for the gamma-glutamyl moiety. Probenecid was also a potent inhibitor of sodium-dependent uptake. S-(1,2-dichlorovinyl)glutathione inhibited sodium-dependent uptake of glutathione in a concentration-dependent manner. Thus, these results show that uptake of DCVG and glutathione is mediated by the same sodium-coupled system. Uptake of S-(1,2-dichlorovinyl)glutathione was also demonstrated in isolated kidney cells; in the presence of sodium, cells accumulated approximately 4-fold more DCVG than in the absence of sodium. This basal-lateral membrane transport system can enable efficient delivery of circulating S-(1,2-dichlorovinyl)glutathione to kidney cells and may, therefore, contribute to its potent and selective nephrotoxicity. In addition, it suggests that renal clearance of glutathione **conjugates** may include transport from the blood through epithelial cells into the lumen as well as direct filtration through the glomerulus.

- L19 ANSWER 139 OF 161 MEDLINE on STN DUPLICATE 54  
85162017. PubMed ID: 3157025. The identification, quantification and possible origin of non-polar **conjugates** in human plasma. Jones D L; James V H. Journal of steroid biochemistry, (1985 Feb) 22 (2) 243-7. Journal code: 0260125. ISSN: 0022-4731. Pub. country: ENGLAND: United Kingdom. Language: English.
- AB The existence and quantification of non-polar **conjugates** of pregnenolone, dehydroepiandrosterone (DHA) and androstenediol in human plasma is described. The plasma level of non-polar pregnenolone **conjugate** is 200% higher than that of pregnenolone but the **conjugates** of DHA and androstenediol are 10 and 5-10% respectively of the plasma levels of the unconjugated steroid. Non-polar pregnenolone **conjugate** concentrations were found to be highly elevated in the plasma of one pregnant subject, and elevated in the plasma of patients with acne and breast cancer. Non-polar DHA **conjugate** levels were significantly elevated in hirsute patients and were approaching significance for patients with acne. A subject taking the combined oral contraceptive pill had very low plasma DHA **conjugate** levels. No significant alterations in the plasma levels of the androstenediol **conjugates** were found. A role for the non-polar **conjugates** in the aetiology of hirsutism and acne is proposed.
- L19 ANSWER 140 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 55  
1985:318370 Document No.: PREV198579098366; BA79:98366. CONVERGENT SYNTHESSES OF 9 DEOXY-12-PHENYLTHIOPROSTANOIDS AND 9 DEOXY-DELTA-8-12-PROSTAGLANDIN D-1 DERIVATIVES. JONES D N [Reprint author]; MEANWELL N A; MIRZA S M. DEP OF CHEMISTRY, THE UNIVERSITY, SHEFFIELD S3 7HF, UK. Journal of the Chemical Society Perkin Transactions I, (1985) No. 1, pp. 145-152. CODEN: JCPRB4. ISSN: 0300-922X. Language: ENGLISH.
- AB **Conjugate** additions of organolithium or organomagnesium compounds, mediated by Cu(I), to 2-phenylthiocyclopent-2-enone, and of enolates of the initial adducts to 2-phenylsulfinyloct-1-en-3-one, provided convergent constructions of the prostanoid framework. Stereospecific introduction of the  $\Delta^{13}$ -double bond by sulfoxide elimination, the elimination of benzenesulfonic acid from 12 $\beta$ -phenylsulfinylprostanoids at room temperature, and the chemoselective reduction of 11-oxo-13-en-15-ones to 11-oxo-13-en-15-ols,

provided 9-deoxy-12-phenylthioprostaglandin D1 analogs and 9-deoxy- $\Delta^8(12)$ -prostaglandin D1 derivatives. The **conjugate** additions, and the propensity for ether formation during the Meerwein-Ponndorf-Verley reduction of the 13-en-15-ones, were influenced by the presence of remote oxygen substituents in the incipient  $\alpha$ -side-chain.

L19 ANSWER 141 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 56

1985:254137 Document No.: PREV198579034133; BA79:34133. **CONJUGATE** ADDITIONS TO ALPHA BETA UNSATURATED SULFOXIDES SYNTHESIS OF CYCLOPENTENONES AND 9 DEOXYPROSTANOIDS. BROWN P J [Reprint author]; JONES D N; KHAN M A; MEANWELL N A; RICHARDS P J. DEP CHEMISTRY, UNIV, SHEFFIELD S3 7HF, UK. Journal of the Chemical Society Perkin Transactions I, (1984) No. 9, pp. 2049-2060. CODEN: JCPRB4. ISSN: 0300-922X. Language: ENGLISH.

AB 1,4-Dicarbonyl compounds, and hence cyclopentenone derivatives [occurring in many compounds of commercial interest, prostaglandins, antibiotics, etc.], were prepared by **conjugate** additions of enolate and related anions to  $\alpha,\beta$ -unsaturated sulfoxides, followed by sulfoxide-ketone transformations. These transformations involved trapping the intermediate  $\alpha$ -sulfinyl carbanions with dimethyl disulfide to give thioacetal monoxide derivatives, or Pummerer rearrangements of the sulfoxides to give alkenyl sulfides. 3-Substituted 2-ethoxycarbonylcyclopentenones prepared in this way were converted into 9-deoxyprostanoids and their 12-ethoxycarbonyl derivatives, the latter by use of 2-phenylsulfinyloct-1-en-3-one as an electrophilic prostanoid  $\beta$ -side-chain precursor.

L19 ANSWER 142 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 57

1985:341996 Document No.: PREV198580011988; BA80:11988. ASPECTS OF THE REPRODUCTIVE ENDOCRINOLOGY OF THE FEMALE GIANT PANDA AILUROPODA-MELANOLEUCA IN CAPTIVITY WITH SPECIAL REFERENCE TO THE DETECTION OF OVULATION AND PREGNANCY. HODGES J K [Reprint author]; BEVAN D J; CELMA M; HEARN J P; JONES D M; KLEIMAN D G; KNIGHT J A; MOORE H D M. INST ZOOL, ZOOL SOC LOND, REGENT'S PARK, LONDON NW1 4RY, ENGL, UK. Journal of Zoology (London), (1984) Vol. 203, No. 2, pp. 253-268. CODEN: JZOOAE. ISSN: 0022-5460. Language: ENGLISH.

AB The metabolism and pattern of excretion of urinary steroids during estrus and pregnancy in the giant panda is described. Three female pandas from the London [UK], Washington [USA] and Madrid [Spain] Zoos were studied over different periods between March 1980 and Sept. 1982. High pressure liquid chromatography and sequential enzyme hydrolysis indicated that estrone glucuronide was the most abundant urinary estrogen metabolite during estrus. Levels of conjugated estrone in late pregnancy were low and similar to those of conjugated estradiol-17 $\beta$ . There was a rapid increase in the excretion of conjugated estrone to reach maximum levels during late proestrus: estrus occurred when levels of conjugated estrone were declining. The measurement of estrone-3-glucuronide by direct, non-extraction assay provides a rapid and reliable method for detecting estrus and ovulation in the giant panda. Artificial insemination of the London and Madrid pandas was performed in 1981 and 1982, respectively. The Madrid panda gave birth to twin cubs after a gestation period of 159 days. Levels of urinary estrone **conjugate** remained low throughout pregnancy. There was no increase in the excretion of pregnanediol-3 $\alpha$ -glucuronide (assumed to be an urinary metabolite of progesterone) until approx. day 120 when a rapid, 5-fold increase in levels occurred. The levels of pregnanediol-3 $\alpha$ -glucuronide remained elevated for approx. 3 wk after which there was a gradual decline beginning 2.5 wk before parturition. Measurement of pregnanediol-3 $\alpha$ -glucuronide enables the detection of pregnancy after 3-4 mo. and should also be useful in predicting parturition. A delay of implantation during pregnancy in the giant panda is suggested. There was no consistent elevation in pregnanediol-3 $\alpha$ -glucuronide excretion in the 5 mo.

after artificial insemination of the London panda, despite a marked increase in circulating progesterone of ovarian origin. Pregnancy could not be confirmed from external examination of the uterus at laparotomy; histological examination of biopsy material revealed advanced endometrial hyperplasia.

L19 ANSWER 143 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 58

1984:258059 Document No.: PREV198477091043; BA77:91043. HYDROLYSIS OF  
PHOSPHATE ESTERS BOUND TO COBALT III KINETICS AND MECHANISM OF INTRA  
MOLECULAR ATTACK OF HYDROXIDE ON COORDINATED 4 NITROPHENYL PHOSPHATE.  
**JONES D R** [Reprint author]; LINDOY L F; SARGESON A M. RES SCH  
CHEM, AUST NATL UNIV, CANBERRA, ACT 2600, AUST. Journal of the American  
Chemical Society, (1983) Vol. 105, No. 25, pp. 7327-7336.  
CODEN: JACSAT. ISSN: 0002-7863. Language: ENGLISH.

AB The hydrolysis of coordinated 4-nitrophenyl phosphate ester in  
cis-[Co(en)2(OH)O3POC6H4NO2] was studied over the pH range 7-14 by 31P NMR  
spectroscopy and by monitoring nitrophenol release at 400 nm.  
Intramolecular attack by 18O-labeled coordinated hydroxide yields  
initially a 5-coordinate phosphorane, which decays to the tris chelate  
[Co(en)2PO4] and nitrophenol ( $k_{obsd} = 7.8 \times 10^{-4} \text{ s}^{-1}$  at 25°  
C in the pH range 9-11.8) with 18O bonded between Co and P. The  
hydrolysis is 105-fold faster than that of the uncoordinated ester under  
the same conditions. At pH 10 there is evidence for 18O exchange between  
solvent and the 5-coordinate phosphorane, and therefore Co.sbd.OH addition  
and ester hydrolysis are not concerted processes. Above pH 11.8, paths  
first and second order in [OH-] dominate. They involve **conjugate**  
base (SN1CB) paths for release of 4-nitrophenyl phosphate by Co.sbd.O bond  
rupture (> 80%) and paths that give small yields of nitrophenol. The  
metal complex reaction is discussed in relation to the hydrolysis of  
 $\beta$ -hydroxyalkyl phosphate esters and possible implications for the  
mechanism of the enzyme Escherichia coli alkaline phosphatase.

L19 ANSWER 144 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

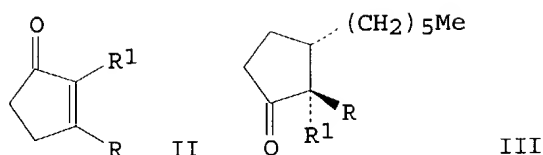
1983:178849 Document No. 98:178849 Chemoselective behavior of enolate  
carbenes derived from dianions of enol thioacetals. Cohen, Theodore;  
**Yu, Lin Chen** (Dep. Chem., Univ. Pittsburgh, Pittsburgh, PA, 15260,  
USA). Journal of the American Chemical Society, 105(9), 2811-13 (English)  
1983. CODEN: JACSAT. ISSN: 0002-7863. OTHER SOURCES: CASREACT  
98:178849.

AB Evidence is provided for the generality of the newly enunciated concept  
that the normally stable lithio derivs. of di-Ph thioacetals decompose  
cleanly to carbenes when another neg. charge is present nearby in the same  
mol.; furthermore, in contrast to conventional carbenes, these carbenes  
can be highly selective in their reactions which are determined by the nature  
of the second anionic site and its juxtaposition with respect to the  
carbenic C atom. When the Li enolate produced by  $\beta$ -addition of  
tris(phenylthio)methyl lithium to 2-cyclohexenone is treated with  
sec-butyllithium at -50°, S-Li exchange occurs and the resulting  
double **conjugate** base of an enol-thioacetal, upon being warmed  
to 0°, decomps. to a Li dienolate which is believed to arise by a  
1,2-H transfer in the intermediate enolate carbene. A similar sequence  
starting with (-)-carvone results in the production of a bicyclo[4.1.0] system  
formally resulting from the addition of PhSCH across the enone double bond.  
The difference in behavior in the two systems is rationalized on the basis  
of conformational differences. Cyclopentenone gives both types of  
products.

L19 ANSWER 145 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1983:438071 Document No. 99:38071 Alkenyl sulfoxides as precursors to  
cyclopentenones and prostanoid  $\beta$ -side chains. Brown, Peter J.;  
**Jones, D. Neville**; Khan, M. Akram; Meanwell, Nicholas A. (Dep.  
Chem., Univ. Sheffield, Sheffield, S3 7HF, UK). Tetrahedron Letters,  
24(4), 405-8 (English) 1983. CODEN: TELEAY. ISSN: 0040-4039. OTHER  
SOURCES: CASREACT 99:38071.

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AB **Conjugate** addition reaction of enolate anions with  $\alpha,\beta$ -unsatd. sulfoxides followed by Pummerer rearrangement, hydrolysis, and cyclization gave cyclopentenones. E.g., addition reaction of  $\text{LiCH:C(OH)Me}$  with  $\text{Me(CH}_2)_5\text{C(:CH}_2)_2\text{S(O)Ph}$  in THF at  $20^\circ$  for 12 h gave 63%  $\text{Me(CH}_2)_5\text{CH[S(O)Ph](CH}_2)_2\text{COMe}$ , which underwent Pummerer rearrangement with  $(\text{F}_3\text{CCO})_2\text{O}$  and pyridine in  $\text{CH}_2\text{Cl}_2$  for 75 min followed by hydrolysis to give 65%  $\text{Me(CH}_2)_5\text{CO(CH}_2)_2\text{COMe}$  (I). Cyclization of I with aqueous  $\text{EtOH/NaOH}$  gave dihydrojasmonone [II;  $\text{R} = \text{Me}$ ,  $\text{R}_1 = (\text{CH}_2)_4\text{Me}$ ]. Reduction of II [ $\text{R} = (\text{CH}_2)_5\text{Me}$ ,  $\text{R}_1 = \text{CO}_2\text{Et}$ ], similarly prepared from the Li/Na dianion of  $\text{MeCOCH}_2\text{CO}_2\text{Et}$ , with  $\text{NaBH}_3\text{CN}$  gave 54% cyclopentanone III ( $\text{R} = \text{CO}_2\text{Et}$ ,  $\text{R}_1 = \text{H}$ ), which underwent addition reaction with  $\text{Me(CH}_2)_4\text{COC(:CH}_2)_2\text{S(O)Ph}$  followed by thermolysis and reduction to give an inseparable mixture of III [ $\text{R} = \text{CH:CHCH(OH)(CH}_2)_4\text{Me}$ ,  $\text{R}_1 = \text{CO}_2\text{Et}$ ;  $\alpha$ -,  $\beta$ -OH], with the  $\alpha$ -OH isomer predominating.

L19 ANSWER 146 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
1982:417096 Document No. 97:17096 Drug-stimulated hydrogen peroxide formation in hepatocytes. Possible toxicological implications. Orrenius, Sten; Thor, Hjoerdis; Ekloew, Lena; Moldeus, Peter; **Jones, Dean P.** (Dep. Forensic Med., Karolinska Inst., Stockholm, S-104 01, Swed.). Advances in Experimental Medicine and Biology, 136A(Biol. React. Intermed.-2, Chem. Mech. Biol. Eff., Pt. A), 395-405 (English) 1982. CODEN: AEMBAP. ISSN: 0065-2598.

AB Drugs such as benzphetamine [156-08-1] and ethylmorphine [76-58-4] stimulate  $\text{H}_2\text{O}_2$  production by the cytochrome P-450 system in isolated rat hepatocytes. The concomitant loss of cellular GSH [70-18-8] appears to be due to enhanced rate of GSSG [27025-41-8] efflux from the cells as a result of glutathione peroxidase functioning in the decomposition of the  $\text{H}_2\text{O}_2$  formed. Lipid peroxidn. and cell damage, which can be the result of  $\text{H}_2\text{O}_2$  accumulation in hepatocytes, are not observed during incubation of hepatocytes with benzphetamine or ethylmorphine, probably because of the antioxidant effect of these drugs. Apparently, other drugs, which lack this property, may cause toxicity by stimulated formation of reduced O species, including the superoxide radical,  $\text{H}_2\text{O}_2$ , and the hydroxyl radical.

L19 ANSWER 147 OF 161 MEDLINE on STN DUPLICATE 59  
80200648. PubMed ID: 7379456. Urinary **conjugates** of 4-hydroxy-3-methoxyphenylethylene glycol do not provide an index of brain amine turnover in man. Boobis A R; Murray S; **Jones D H**; Reid J L; Davies D S. Clinical science (London, England : 1979), (1980 Apr) 58 (4) 311-6. Journal code: 7905731. ISSN: 0143-5221. Pub. country: ENGLAND: United Kingdom. Language: English.

AB 1. The 24 h urinary excretion of free 4-hydroxy-3-methoxyphenylethylene glycol (HMPG), HMPG conjugated as glucuronide and HMPG conjugated as sulphate was determined in nine healthy volunteer subjects and six patients with phaeochromocytoma. In both groups of subjects most (97%) HMPG was in the conjugated form. 2. Although patients with phaeochromocytoma excreted five- to ten-fold the amounts of each of the forms of HMPG excreted by the control subjects the ratio of these different forms of HMPG to each other did not differ significantly between the groups. 3. In cerebrospinal fluid and brain about 80% of HMPG was free and of the conjugated HMPG in these two tissues most was in the glucuronide form. 4. It is concluded from these data that both HMPG

sulphate and HMPG glucuronide have a substantial peripheral origin and that measurements of their urinary excretion cannot be used as an index of brain catecholamine turnover.

- L19 ANSWER 148 OF 161 MEDLINE on STN DUPLICATE 60  
79151005. PubMed ID: 429318. Metabolism of glutathione and a glutathione **conjugate** by isolated kidney cells. **Jones D P**; Moldfus P; Stead A H; Ormstad K; Jornvall H; Orrenius S. Journal of biological chemistry, (1979 Apr 25) 254 (8) 2787-92. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.
- L19 ANSWER 149 OF 161 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 61  
79161960 EMBASE Document No.: 1979161960. Use of isolated kidney cells for study of drug metabolism. **Jones D.P.**; Sundby G.B.; Ormstad K.; Orrenius S.. Dept. Forens. Med., Karolinska Inst., S-104 01 Stockholm, Sweden. Biochemical Pharmacology 28/6 (929-935) 1979. CODEN: BCPA6. Pub. Country: United Kingdom. Language: English.
- AB Isolated kidney cells were prepared from rat kidneys using a recirculating perfusion system with collagenase. The preparation was rapid and provided a high yield of intact metabolically active kidney cells predominantly of tubular origin. The respiration rate was 2.7  $\mu\text{mol O}_2/\text{hr}$  per 106 cells and was not stimulated by ADP. GSH content was 28.9 nmol/106 cells and did not decline during 2 hr of incubation. Cytochrome P450 content was 0.064 nmol/106 cells. The cells were characterized for their drug metabolizing activity using paracetamol as substrate. The rate of formation of the glucuronide and sulfate derivatives was linear for 2 hr, but slower than previously reported for rat liver cells. In contrast to incubation with liver cells, no glutathione **conjugate** was detected. However, formation of both cysteine and N-acetylcysteine derivatives was observed. The rate of formation of total sulphydryl **conjugates** was about 50% of that reported for liver cells when expressed on a cytochrome P450 basis. These studies establish the reliability and utility of this cell preparation as a model system for the study of drug metabolism by the kidney.
- L19 ANSWER 150 OF 161 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 62  
79142753 EMBASE Document No.: 1979142753. Histamine receptors on guinea-pig alveolar macrophages: Chemical specificity and the effects of H1- and H2-receptor agonists and antagonists. Diaz P.; **Jones D.G.**; Kay A.B.. Dept. Pathol., Med. Sch., Edinburgh EH8 9AG, United Kingdom. Clinical and Experimental Immunology 35/3 (462-469) 1979. CODEN: CEXIAL. Pub. Country: United Kingdom. Language: English.
- AB Various guinea-pig leucocytes were tested for their capacity to bind histamine coupled as a rabbit serum albumin **conjugate** (H-RSA) to formalised ox red cells. The percentage of rosette-forming target cells was directly related to the concentration of erythrocyte-bound H-RSA. Under optimal experimental conditions the numbers of rosettes varied from 60 to 81% for alveolar macrophages, 14 to 73% for peritoneal macrophages, 14 to 30% for blood monocytes, 27 to 48% for lymph node cells, 7 to 24% for blood lymphocytes and 0 to 29% for peritoneal and blood neutrophils. Virtually no histamine rosettes were forming with eosinophils or basophils. Free histamine partially inhibited rosette formation by alveolar macrophages in a dose-dependent fashion from 10<sup>-3</sup> to 10<sup>-5</sup> mol/l, and complete inhibition was achieved by the H-RSA **conjugate**. In contrast, amines closely related to histamine such as L-histidine and the major histamine catabolites, imidazoleacetic acid, 1,4-methylhistamine, 1-methyl-4-imidazoleacetic acid and N-acetylhistamine, had no inhibitory effect. The histamine H1-receptor antagonists, mepyramine and chlorpheniramine, and the H1-receptor agonist, 2-(2-aminoethyl) thiazole, all inhibited rosette formation by alveolar macrophages in a dose-dependent fashion. However, the H2-receptor antagonists, burimamide and metiamide, and the H2-receptor antagonists, Dimaprit and 4-methyl-histamine, were inactive. These experiments suggest that compared

to other leucocytes, histamine receptors are particularly well expressed on the alveolar macrophage, these receptors have a high degree of specificity for histamine in that other amines, closely related chemically, did not inhibit rosette formation, and the binding of histamine to the alveolar macrophage membranes is H1-and not H2-receptor dependent.

L19 ANSWER 151 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN

1979:517699 Document No. 91:117699 Histamine-coated particles generate superoxide (O<sub>2</sub><sup>-</sup>) and chemiluminescence in alveolar macrophages. Diaz, Patricia; Jones, D. G.; Kay, A. B. (Med. Sch., Univ. Edinburgh, Edinburgh, UK). Nature (London, United Kingdom), 278(5703), 454-6 (English) 1979. CODEN: NATUAS. ISSN: 0028-0836.

AB O<sub>2</sub><sup>-</sup> formation by isolated guinea pig alveolar macrophages (used as a measure of the respiratory burst) was not stimulated by histamine (I) [51-45-6] (10<sup>-3</sup> mol/L) but was stimulated by rabbit serum albumin (RSA)-bound I adsorbed onto zymosan particles (a yeast cell wall extract). Other particles, e.g. crosslinked dextrose gel (Sephacrose 4B) could be used instead of zymosan. The amount of O<sub>2</sub><sup>-</sup> generated was directly proportional to the quantity of I-RSA **conjugate** added to the particles; O<sub>2</sub><sup>-</sup> formation was much less when the **conjugate** was not adsorbed onto particles. Serum (as a source of complement)-coated zymosan caused stimulation similar to that produced by the **conjugate**-coated particles. Stimulation by bound I was mediated by H1- and H2-receptors on the alveolar macrophages. Chemiluminescence, which also accompanied the respiratory burst of phagocytic cells, was initiated by bound I. This effect was completely inhibited by superoxide dismutase, indicating that light emission by these cells was closely associated with O<sub>2</sub><sup>-</sup> production

L19 ANSWER 152 OF 161 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 63

1979:78122 Document No.: PREV197917018122; BR17:18122. GLUTATHIONE AND GLUTATHIONE **CONJUGATE** METABOLISM IN ISOLATED LIVER AND KIDNEY CELLS. JONES D P; STEAD A H; MOLDEUS P; ORRENIUS S. Hoppe-Seyler's Zeitschrift fuer Physiologische Chemie, (1978) Vol. 359, No. 9, pp. 1040. CODEN: HSZPAZ. ISSN: 0018-4888. Language: Unavailable.

L19 ANSWER 153 OF 161 MEDLINE on STN

78121392. PubMed ID: 629318. Serum concentration of bile acids in relation to the normal menstrual cycle the administration of oral contraceptives, and pregnancy. Jones D E; Miranda R; Wolfe M; Demers L M. American journal of obstetrics and gynecology, (1978 Mar 1) 130 (5) 593. Journal code: 0370476. ISSN: 0002-9378. Report No.: PIP-780622; POP-00044817. Pub. country: United States. Language: English.

AB The effects of endogenous and exogenous steroids on serum levels of bile acid glycine **conjugates** were investigated by measuring these serum levels in 10 healthy women during normal menstrual cycle, in 10 healthy women during a cycle of combination oral contraceptives (OCs) (50-100 mcg of ethinyl estradiol or mestranol), and in 27 healthy women during normal pregnancy. Peripheral venous blood was obtained from nonpregnant patients on Days 2, 6, 12, 18, and 24 after onset of uterine bleeding. No significant differences in glycocholic and glycochenodeoxycholic acid serum levels occurred at any point in the cycle. Similarly, no significant differences were noted between patients receiving OCs and those with normal menstrual cycles. Fasting peripheral blood samples from the 27 pregnant volunteers (collected throughout the 3 trimesters) also revealed no significant serum level differences during any trimester. Physiologic changes in endogenous estrogens and progesterones have no appreciable effect on the bile acid serum levels measured; nor, apparently, do moderate doses of synthetic estrogens in OCs alter bile acid serum levels in healthy women.

- L19 ANSWER 154 OF 161 MEDLINE on STN DUPLICATE 64  
 79020937. PubMed ID: 697808. Formation and metabolism of a glutathione-S-**conjugate** in isolated rat liver and kidney cells. Moldeus P; Jones D P; Ormstad K; Orrenius S. Biochemical and biophysical research communications, (1978 Jul 14) 83 (1) 195-200. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.
- L19 ANSWER 155 OF 161 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN  
 78:319992 The Genuine Article (R) Number: FH910. FORMATION AND METABOLISM OF A GLUTATHIONE-S-**CONJUGATE** IN ISOLATED RAT-LIVER AND KIDNEY CELLS . MOLDEUS P (Reprint); JONES D P; ORMSTAD K; ORRENIUS S. KAROLINSKA INST, DEPT FORENS MED, S-10401 STOCKHOLM 60, SWEDEN (Reprint). BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS (1978) Vol. 83, No. 1, pp. 195-200. Pub. country: SWEDEN. Language: ENGLISH.
- L19 ANSWER 156 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 1979:488142 Document No. 91:88142 Glutathione and glutathione **conjugate** metabolism in isolated liver and kidney cells. Jones, D. P.; Stead, A. H.; Moldeus, P.; Orrenius, S. (Dep. Forensic Med., Karolinska Inst., Stockholm, 10 401/60, Swed.). Funct. Glutathione Liver Kidney, [Pap. Konf. Ges. Biol. Chem.], 25th, 194-200. Editor(s): Sies, Helmut; Wendel, Albrecht. Springer: Berlin, Ger. (English) 1978. CODEN: 40SNAF.
- AB The metabolism of extracellular glutathione and paracetamol-S-glutathione **conjugate** was studied in isolated liver and kidney cells. With kidney cells, but not with liver cells, added reduced glutathione (GSH) is rapidly oxidized. The oxidation is O-dependent and yielded oxidized (GSSG), which was the substrate for subsequent degradative reactions. GSSG was only slowly metabolized by liver cells, but this activity is increased following pretreatment with phenobarbital. By comparison, the rate in untreated kidney cells is considerably higher. Anal. of the metabolites by high-pressure liquid chromatog. suggested that the preferred route of GSSG breakdown included removal of a  $\gamma$ -glutamyl residue, removal of the glycyl residue from the cysteinylglycine moiety, removal of the 2nd  $\gamma$ -glutamyl residue, and removal of the 2nd glycyl residue to yield cystine. Upon incubation of liver cells with paracetamol, the GSH consumed was nearly quant. recovered as the glutathione derivative Addition of isolated kidney cells to the liver incubate results in conversion of this metabolite to the cysteine and N-acetylcysteine derivs. This conversion was inhibited by addition of GSSG. Addition of alanyl glycine, a substrate for the peptidase which hydrolyzes cysteinylglycine, resulted in accumulation of another intermediate, paracetamol-S-cysteinylglycine. Thus, the reaction sequence in metabolism of glutathione **conjugates** appears to be the same as that for glutathione breakdown.
- L19 ANSWER 157 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 1972:471974 Document No. 77:71974 Chemical modification of carboxypeptidase A crystals. Azo coupling with tyrosine-248. Johansen, J. T.; Livingston, D. M.; Vallee, B. L. (Dep. Biol. Chem., Harvard Med. Sch., Boston, MA, USA). Biochemistry, 11(14), 2584-8 (English) 1972. CODEN: BICHAW. ISSN: 0006-2960.
- AB Coupling of bovine carboxypeptidase A crystals with diazotized p-arsanilic acid modifies one tyrosyl residue. CNBr cleavage of the enzyme and separation of the resultant fragments demonstrates virtually complete incorporation of the arsanilazo label into segment F1 containing residues 104-301. This fragment was solubilized by succinylation, digested with chymotrypsin, and the arsanilazotyrosyl-containing peptide was isolated by affinity chromatog. using an antibody-Sepharose **conjugate** specific for the arsanilazotyrosyl moiety. The arsanilazotyrosyl peptide was purified by subsequent ion-exchange chromatog. and recovered in 90% overall yield. Its amino acid composition, N-terminal threonine, and tryptophan content are uniquely compatible with the sequence of carboxypeptidase A containing residues 246-257 (Thr-Ile-Tyr-Gln-Ala-Ser-Gly-Gly-Ser-Ile-Asp-Trp). Tyrosine-248 is the residue labeled specifically by diazotized p-arsanilic acid in carboxypeptidase A crystals.

- L19 ANSWER 158 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 1970:100429 Document No. 72:100429 o-Quinonoid compounds. III.  
 Benzopyran-3-ones and their salts. Holland, J. M.; **Jones, David William** (Dep. Org. Chem., Univ. Leeds, Leeds, UK). Journal of the Chemical Society [Section] C: Organic (4), 336-40 (English) 1970. CODEN: JSOAX. ISSN: 0022-4952.
- AB In boiling Ac2O, o-formylphenylacetic acid (I) is partly dehydrated to benzopyran-3-one, which forms appropriate adducts with dienophiles. In H2S 4, I is completely converted into the **conjugate** acid of benzopyran-3-one. Expts. leading to 1-methyl-benzopyran-3-one, the more stable 1-phenyl derivative, and their **conjugate** acids are described.
- L19 ANSWER 159 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 1969:509426 Document No. 71:109426 Relation between C19- and C21-steroid synthesis in the human adrenal gland. Cameron, Euan Hamish Donaldson; Jones, Tom; **Jones, Dilys**; Anderson, Anne Barbara Michie; Griffiths, Keith (Welsh Nat. Sch. Med., Cardiff, UK). Journal of Endocrinology, 45(2), 215-30 (English) 1969. CODEN: JOENAK. ISSN: 0022-0795.
- AB As part of a continuing study of adrenal steroids in relation to breast cancer, various expts. were performed in order to study relations between androgen and corticosteroid biosynthesis. Chopped tumor tissue from a "mixed cell" adrenal adenoma (7.4 g.) was incubated with pregnenolone-4-14C and 17 $\alpha$ -hydroxypregnenolone - 7 $\alpha$ -3H for periods of time ranging 30-120 min. 17 $\alpha$ -Hydroxyprogesterone may not be an obligatory intermediate in androgen or cortisol synthesis. Evidence from further expts. with "normal" human adrenal tissue removed from breast cancer patients using previously established ultramicrochem. techniques indicates that the dehydroepiandrosterone sulfokinase enzyme system is confined to the zona reticularis of the gland. The conversion of dehydroepiandrosterone-7 $\alpha$  - 3H sulfate, androstenedione-7 $\alpha$ -3H and testosterone-7 $\alpha$ -3H to estrogens and their **conjugates** by adrenal homogenates was also investigated. Conversions were extremely low from all precursors.
- L19 ANSWER 160 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 1968:36558 Document No. 68:36558 Individual quantitative estimation of bile acid **conjugates** in normal and lithogenic bile. **Jones, Denzil Dilwyn** (Charing Cross Hosp. Med. Sch., London, UK). Clin. Chim. Acta, 19(1), 57-62 (English) 1968.
- AB A method is described where conjugated bile salts may be quant. estimated after adsorption chromatog. on silicic acid. The method is applicable to hepatic or gallbladder bile. Excellent resolution of the bile salts was obtained. The accuracy and precision of the technique were good.
- L19 ANSWER 161 OF 161 CAPLUS COPYRIGHT 2004 ACS on STN  
 2004:380342 Oxidation of Raloxifene to Quinoids: Potential Toxic Pathways via a Diquinone Methide and o-Quinones. **Yu, Linning**; Liu, Hong; Li, Wenkui; Zhang, Fagen; Luckie, Connie; Van Breemen, Richard B.; Thatcher, Gregory R. J.; Bolton, Judy L. (Department of Medicinal Chemistry and Pharmacognosy College of Pharmacy, University of Illinois at Chicago, Chicago, IL, 60612-7231, USA). Chemical Research in Toxicology ACS ASAP (English). CODEN: CRTOEC. ISSN: 0893-228X. Publisher: American Chemical Society.
- AB Raloxifene was approved in 1997 by the FDA for the treatment of osteoporosis in postmenopausal women, and it is currently in clin. trials for the chemoprevention of breast cancer. Before widespread use as a chemopreventive agent in healthy women, the potential cytotoxic mechanisms of raloxifene should be investigated. In the current study, raloxifene was incubated with GSH and either rat or human liver microsomes, and the metabolites and GSH **conjugates** were characterized using liquid chromatog.-tandem mass spectrometry. Raloxifene was converted to raloxifene diquinone methide GSH **conjugates**, raloxifene o-quinone GSH **conjugates**, and raloxifene catechols. For



comparison, three raloxifene catechols were synthesized and characterized. In particular, 7-hydroxyraloxifene was found to oxidize to the 6,7-o-quinone. As compared with raloxifene diquinone methide, which has a half-life of less than 1 s in phosphate buffer, the half-life of raloxifene 6,7-o-quinone was much longer at  $t_{1/2} = 69 \pm 2.5$  min. The stability offered by raloxifene 6,7-o-quinone implies that it may be more toxic than raloxifene diquinone methide. Cytotoxicity studies in the human breast cancer cell lines S30 and MDA-MB-231 showed that 7-hydroxyraloxifene was more toxic than raloxifene in both cell lines. These results suggest that raloxifene could be metabolized to electrophilic and redox active quinoids, which have the potential to cause toxicity in vivo.

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y

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	ENTRY	SESSION
FULL ESTIMATED COST	651.93	652.14
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
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